Medical
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American Journal of Obstetrics and Gynecology

VOL. XXI ST. LOUIS, JANUARY, 1931 No. 1

Original Communications

AGE PERIOD CHANGES IN THE CERVIX UTERI WITH SPECIAL REFERENCE TO CANCER DEVELOPMENT*

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INTRODUCTION

THE characteristic histologic structure of the cervix uteri with its two distinct types of lining epithelium and tortuous racemose glands dipping down into the stroma, introduces into its tissue constitution a peculiar susceptibility to cell disturbances. Moreover, its physiologic history and the traumas and "chronic inflammations," to which it is particularly exposed after parturition, furnish the necessary internal and external factors for abnormal and atypical growths. It is therefore not surprising to note the frequent occurrence of cancer in the cervix. The corpus uteri, possessing only one characteristic epithelium with a tubular type of gland, fulfilling a more constant and uniform function, is apparently not apt to develop atypical qualities.

Authorities are agreed that the uterus is the most frequent location of all cancers occurring in women, and that the cervix is most commonly involved. About one-third of all female atypical tumors are cervical cancers. Ewing,[1] Peterson,[2] and Anspach[3] find that about 90 per cent of cancers of the uterus occur in the cervix.

It has been quite definitely established by clinical evidence, that an endocervicitis is the forerunner of cervical cancer, although this is not yet fully accepted by pathologists. In the so-called "precancers" very suggestive pictures of potential cancers and incipient cancers

*From a thesis presented in partial fulfilment of the requirements for the degree, Master of Science in Pathology, McGill University, September 1928.

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have been shown, but there has not been demonstrated a fully conclusive sequence from normal tissue into genuine cancer.

The cervix, therefore, assumes a very important rôle in cancer prophylaxis, particularly since it is so much more readily accessible for frequent examination as compared with the corpus.

In this paper a detailed histologic study has been made of cervices of the different age periods, so as to gain a comparative view of the cell changes and their possible connection with the histogenesis of early cancer. No emphasis, therefore, is laid on the demonstration of actual cancerous tissue, but rather on the events leading up to its development. Particular attention is of course given to the epithelial linings and glands, and less consideration to the other parts of the cervix.

TECHNIC AND MATERIAL

Routine examination of cervices has been made but the material for this study does not necessarily come from consecutive patients, as some was derived from autopsy subjects and some from specimens removed for various surgical reasons. Sections were stained in hematoxylin-eosin, following the usual laboratory procedures. No study has been made of the specimens grossly, as only the histology has been considered. Care has been taken to overrule artefacts caused by sections being cut at various planes. This has been done by the study of serial sections (about every tenth one being stained) and by careful differential diagnosis of the cells.

In all, 124 specimens have been stained, 24 autopsy cervices, and 100 surgical cases, chiefly inflammatory. They have been arranged according to the various age periods; viz., 1, fetal; 2, infantile; 3, adult, and 4, senile. Examined according to age, there were as follows:

1st decade	7 specimens
2nd decade	2 specimens
3rd decade	15 specimens
4th decade	49 specimens
5th decade	31 specimens
6th decade	13 specimens
7th decade	7 specimens
	124

RESULTS

1. *Fetal Period.*—The fetus well illustrates the many evolutionary aspects which the lining membrane of the portio and the endocervix present even before birth. Indeed it is an early example of the remarkable instability of the cervical lining membrane and the facility of interchangeability or metaplasia of its two types of cells.

During the first months of intra-uterine life there is no differentiation in the lining epithelium between the uterus and vagina; and the

portio is not in existence. About the fourth or fifth month there is an evolution of the vaginal epithelium into the squamous type, and this gradually progresses upward until the lower part of the cervix has been penetrated by squamous epithelium.

From the sixth month on, the cervix begins to assume its characteristic mucous epithelium, and this gradually pushes out the invading squamous tissue from inside of the cervix. Thus the dividing line between the columnar and squamous types of cells comes to lie at the external os. In this process of differentiation, a series of abnormalities can appear. Thus, rests of basal squamous epithelium may remain behind the mucous lining and later, according to the investigations of some writers, can undermine the columnar epithelium and produce so-called "metaplasias." Also the squamous epithelium may remain

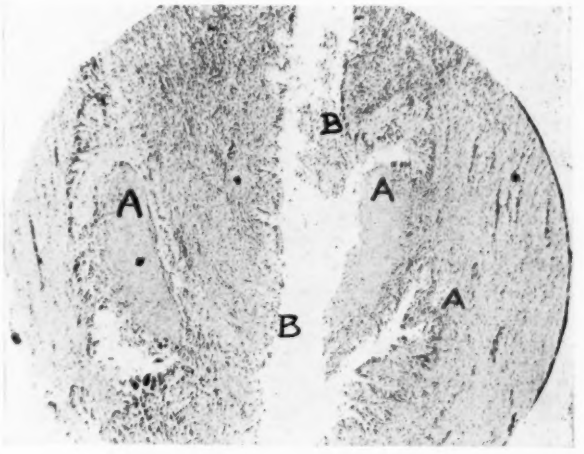

Fig. 1.—Cervix from infant three days old. View of endocervical portion. Illustrates a persistence at birth of an abnormality in fetal evolution, in which invading squamous epithelium, growing in from below as usual, has penetrated the endocervix deeply, remained behind, but has not been displaced by the downgrowing mucous epithelium of the cervix. *A*, is the persistent squamous epithelium of the portio, replacing *B*, the typical mucous columnar epithelium of the endocervix.

intact inside the cervix for a considerable distance upward, passing the usual boundary line of the external os. The columnar epithelium in its downward path sometimes oversteps the external os and reaches the portio (congenital erosion). (See Fig. 1.)

Fischel[4] found these congenital erosion patches to possess crypts and glands, thus proving them definitely developmental malformations. He believed that these remains could continue on in later life and be the basis for the formation of adult erosions.

2. *Infantile Period.*—Compared to the adult, at birth the lining epithelium of the endocervix shows relatively higher columnar cells with their nuclei removed some distance from the basement membrane; the glands are fewer in number.

A variable time later on in infancy the columnar cells begin to assume the adult appearance. In this series in sections from infants three weeks old, there is noticed in parts a descent of the nucleus toward the base of the cell, although for the most part the cells are still infantile in character; while at two and a half months of age the fully developed adult type is apparent.

3. *Adult Period.*—Under this heading can be grouped from a histologic viewpoint the prepuberty, puberty, nonpregnant, and pregnant adult cervices up to the menopause. There is little direct effect by these various physiologic influences on the cervix, which is inactive and receives only passive results.

During menstruation the cervix is unchanged. In pregnancy, the connective tissue becomes softened and the muscle fibers become longer, with the cervical glands secreting more mucus (Frank[5]). Williams[6] attributes the slight increase in size of the cervix to the increased hyperemia and notes very little hypertrophy of the muscle fibers.

Although pregnancy in itself does not materially alter the cervix, the after-effects of parturition are very important and far-reaching as regards the genesis and development of cancer.

Williams[6] states that slight degrees of cervical laceration must be regarded as an accompaniment of childbirth. Blair Bell[7] notes lacerations in many cases of so-called normal labor. DeLee[8] is astonished at the amount of damage even normal labor causes, and amazed at the complicity of the injuries. Danforth[9] admits that nearly all, if not all, women who bear children suffer some injury to the cervix.

Most cervical lacerations become infected and produce a cervicitis with its consequent evils. They need only be mentioned here, leucorrhea, eversion, ectropion, erosion, hyperplasias of the epithelium and glands, cyst formation, etc. Thus, it is evident that following labor, a normal physiologic process, most women receive lacerations and attendant endocervicitis. Therefore, the occurrence of endocervicitis can almost be considered a usual event in childbearing women.

Peterson[2] has worked out the age distribution in his series of 406 cancers of the cervix. Most of the cases occur between the ages of thirty-five and forty-five, when pregnancy and labor have already taken place and have left their sequelae behind. O'Brien[10] remarks that at this age of life only 9.16 per cent of women have not been married. Kelly[11] noted that 98 per cent of his series of squamous cancers of the cervix had histories of previous childbirth. Cullen[12] in 50 cases of squamous-celled carcinoma of the cervix found that only one had not been through labor. It is pointed out by many writers that the number of pregnancies does not influence the occurrence of cancer of the cervix, but that the actual incident of a single labor is sufficient. Polak[13] quotes Graves's findings of 91 per cent incidence of obstetric trauma preceding 538 cases of cancer of the cervix. He contrasts these results with a study of the hospital records of 4,815 cervical repairs, which included the operations of trachelorrhaphy, amputation, and cauterization. It was found that only 7 of these patients later developed cancer, and in

3 of them malignant changes were already present in the tissue at the time of the primary operation.

Chronic endocervicitis is generally recognized as a great factor in the production of cancer. Cancer of the cervix was preceded by chronic endocervicitis in 34 out of 48 cases (Polese[14]). Polak[15] makes the statement that "long-continued cervical inflamamtion may be considered a prodrome of cervical cancer, for it is but a step from the extreme cell proliferation with an orderly arrangement that occurs in hyperplastic endocervicitis and cervicitis, to the disorderly arrangement of embryonal cells found in cancer." C. J. Miller[16] believes that "endocervicitis is a condition to which may be truly applied that much-abused word, precancerous." Warthin[17] upon examination of the cervix in several unmarried women who had previously received repeated traumas of this organ for a number of years through

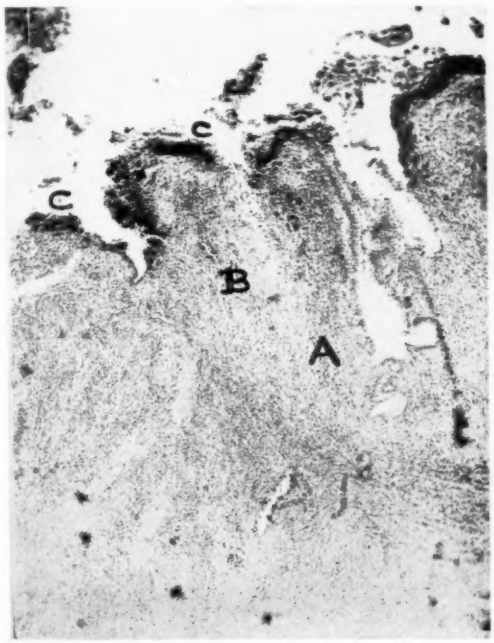

Fig. 2.—Cervix, patient aged sixty-eight. Erosion. Various stages of this condition are seen. As a result of severe inflammation, the stratified squamous lining of the portio has become macerated and is missing, *C*. The new columnar layer destined to cover the denuded subepithelial tissue temporarily has not developed as yet. A later stage of healing in which new squamous epithelium is overcoming the newly formed glands is seen at *A* and *B*.

treatment by medical men, found "all sorts of early precancerous conditions, inflammatory hyperplasias, atypical regenerations, and metaplasias, up to fully developed carcinomas."

Although chronic endocervicitis may be caused by other etiologic factors, it is accepted that the most frequent cause is the trauma and lacerations of labor with consequent infection. The other causes of infection are chiefly gonorrheal and those of pyogenic bacterial origin. Hess[18] regards gonorrheal vulvovaginitis in children as involving the cervix rather than the vagina. When one considers that the uterus from the fundus to the external os is germ-free (Barbour[19]), while the

vagina does harbor germs, it can readily be appreciated why the traumas of labor cause most pathologic conditions in the cervix. Endocervicitis is a very frequent condition, as 85 per cent of all women, single or married, have infected cervices (Polak[15]).

In our series, most of the patients examined had developed endocervicitis. These inflammatory cervices have been grouped, for purposes of study, under the following subdivisions: viz., A, erosion of the cervix; B, epidermidalization (metaplasia); C, hyperplasia of the squamous epithelium, and D, hyperplasia of the glands.

A. Erosion of the Cervix.—Exclusive of the congenital type the adult erosions, according to Adair,[20] occur very frequently during labor. Out of 102 patients with normal labors, who were later examined by Kerwin,[21] he found 21 showing marked cervical erosions.

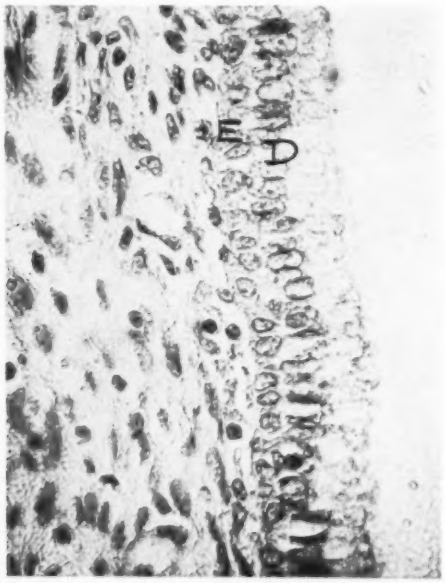

Fig. 3.—Cervix, patient aged thirty-nine. Illustrating the first step in the process of epidermidalization (metaplasia of columnar epithelium). High-power view. Between the original columnar cells, *D* and the basement membrane is noticed a new layer of polygonal cells, the infraepithelial cells, *E*.

These erosions showed various stages, the first being the loss of the portio squamous epithelium, resulting from the inflammation, thus exposing the subepithelial tissue. Underneath is a true picture of inflammation with many new glands formed. In the second stage occurs the first attempt at healing, and the ulcerated area is covered with true columnar epithelium which can better withstand the effects of the discharge. Soon squamous epithelium grows in from the margins and in the third stage there is final healing, consisting of an overrun of squamous epithelium into the glands and underneath the columnar tissue undermining it. The glands may become filled com-

pletely with solid plugs of squamous epithelium or their openings may be blocked, producing cysts. Finally, the filled glands flatten out and merge with the squamous layer, and thus the ulcer is completely bridged over. (See Fig. 2.) Thus, the erosion is a curious and loose mixture of squamous and columnar epithelium.

Several authors hold that an erosion can become cancerous through overgrowth of the new squamous epithelium. Eden and Ley[22] conclude: "It will probably become in time established that it is the erosion which is accompanied by deep cervical lacerations, by thickening and eversion of the lips of the cervix, and histologically by abundant round-celled infiltrations, which is most liable to become

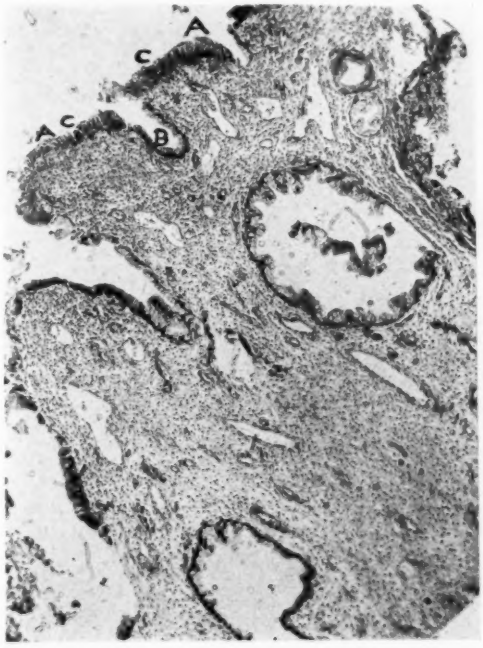

Fig. 4.—Cervix, patient aged twenty-nine. Later stage of epidermidalization. Increasing stratification at *C*, with differentiation into the flat desquamating type at *A*. Note how abruptly the normal columnar epithelium, *B*, joins the infraepithelial cell patches.

cancerous. The form which occurs in nulliparous women is probably more benign." Ewing has noted early cancerous overgrowth of the edges of a chronic erosion, and he believes cervical erosion to be the most definitely established lesion known to precede cervical cancer.[23] Rubin[24] discusses three cases of early cancer beginning in healing erosions. Stone[25] mentions several investigators who have the same views on the origin of portio cancers from erosions. Polak[26] holds that cervical erosion is a constant precursor of cancer.

B. Epidermidalization and Epidermoidalization (Metaplasia) of Columnar Epithelium and Glands.—By this is meant a change from the

single-layered columnar type of cervical epithelium into several layers of squamous tissue closely resembling that of the portio. Because of the doubt of origin of these new layers Fluhmann[27] discourages the use of the terms "metaplasia of cylindrical epithelium" or "stratification of cylindrical epithelium." He stresses the adoption of the description "epidermidalization" when the stratification is normal in appearance, and the term "epidermoidalization" when the layers are atypical. This terminology is accepted in this paper. These changes can take place either on the surface of the endocervix or in the glands proper. Cases where glands or stroma have been overcome by hyperplasia of the lining squamous epithelium

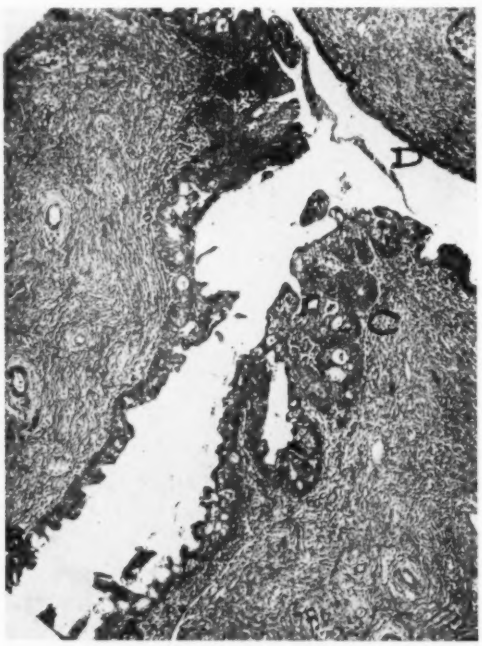

Fig. 5.—Cervix, patient aged forty. Epidermoidalization process. Excessive atypical overgrowth of new squamous cells along the walls of a large duct, penetrating into glands and overcoming them; and also dipping down into the stroma. At *A* and *B* a view is given of the beginning of the process, with new cells piling up under the columnar epithelium normally lining the duct. Further up at *C* is the increasing stratification in glands and stroma. These masses of cells consist of an outer rim of prickle cells with a central collection of flat desquamating cells. The unaffected duct lining is shown at *D*. Picture is suggestive of a carcinoid condition.

which has penetrated deeply are not included in this subdivision but are studied later under the heading of "hyperplasia of the squamous epithelium." It is possible, however, to have in the same section examples of the so-called metaplasias and squamous hyperplasias.

The stratification develops layer upon layer, although it is irregular in tempo of growth. Thus various stages of epidermidalization can be seen at one and the same time in the field examined. The most frequent appearance is that resembling a piling-up of the cells of the

lowest layer of squamous epithelium, the basal-celled layer. (See Figs. 3 and 4.)

In some cases the epidermidalization formation becomes greatly exaggerated. There results a remarkable proliferation of dense masses of squamous epithelium which are definitely atypical and suggestive of the "precancer" state. (See Fig. 5, which illustrates "epidermoidalization.")

If one accepts the view that epidermoidalization is a precancerous state, the milder cases of epidermidalization can be explained as the earliest stages in the development of potential squamous-celled carcinoma.

Fig. 6.—Cervix, patient aged forty-five. Squamous epithelium hyperplasia and downgrowth. Note the epidermized glands, *A*, the masses of ingrowing squamous epithelium, *B*, and the various unaffected columnar parts, *C*.

There is noticeable in these cases, both types, an inflammatory condition or cervicitis. This seems to be the exciting factor for the production of these new cells. Fluhmann[27] found cervicitis to be present in every case of epidermidalization he examined. In 1195 consecutive specimens of the cervix uteri he found 59 cases of epidermidalization in various stages of development. In this series of 124 specimens there were 15 cases of epidermidalization and epidermoidalization, all occurring in cervicitis.

Fluhmann[27] gives a very good summary of the various theories advanced for the genesis of the new layers of cells concerned in epidermidalization. According to Eichholz[28] and Frankl,[29] they originate from the basal cells of near-by squamous

epithelium. Against this theory is the occurrence of epidermidalization at the tips of polyps and deep in glands where no adjacent squamous epithelium is present. Robert Meyer[30] believes that congenital nests of squamous epithelium left underneath the columnar epithelium undergo new growth and substitute the cylindrical epithelium. Kaufmann[31] and Oeri[32] in 1906 concluded that there was a definite metaplasia of the cylindrical into squamous epithelium and that these infraepithelial cells were a transitional phase.

Eichholz[28] and Geller[33] also presume that certain embryonic undifferentiated cells can be included in cylindrical epithelium and possess the potentiality of developing into either type of tissue. Krompecher[34] believes that cylindrical epithelium possesses a basal-cell layer which is embryonic and can differentiate into squamous epithelium.

C. Hyperplasia of the Squamous Epithelium.—In this instance there is an increase in the cells of the various layers of the portio squamous

Fig. 7.—Cervix, patient aged thirty-three. Epidermization of gland through excessive downgrowth of surface squamous epithelium. At *A* there is marked proliferation of squamous cells into rupture through the basement membrane. The cells here are beginning to assume an abnormal appearance. The picture is that of a carcinoid change.

epithelium. As a result the undulating lower border of the epithelium becomes very irregular through downgrowth into the stroma. All stages of hyperplasia can be seen, from the simplest with small flat papillary downgrowths to the extensive showing extremely long pegs of squamous epithelium invading the deeper layers of the stroma and overcoming glands. It is these severer grades of hyperplasia that may possess some of the attributes of cancer, and are definitely labelled precancerous by many writers.

The squamous epithelium replaces the columnar epithelium of the surface or glands by direct extension and thus differs from the process

of epidermidalization previously described. Some of the sections, however, show the two conditions existing on the same slide. (See Figs. 6, 7 and 8.)

From these sections, it is not difficult to understand how the elongated pegs of squamous epithelium could infiltrate the stroma in the malignant fashion upon further irritation.

Several of the hyperplastic specimens examined exhibit a horny layer, which normally is absent. None of the sections show any pearl formation.

The condition of squamous epithelium hyperplasia and downgrowth seems to be a frequent one. Including mild cases of hyperplasia there

Fig. 8.—Cervix, patient aged thirty-four. Papilloma of the cervix. Illustrative of a leukoplakia condition. Extraordinary broadening of the squamous layers, the epithelium being about six times as broad as the normal lining. *A*, upper border of squamous epithelium; *B*, lower border; *C*, overshadowed stroma.

were found in this series of 124 cases, 29 such specimens. The etiologic factor at the base of these hyperplasias is cervicitis and this is very evident histologically.

White and Weidman[35] studied epidermal hyperplasia at the margins of cutaneous ulcers, and concluded that "every gradation of hyperplasia occurs among such ulcers, even to those which mimic early epithelioma perfectly as expressed histologically."

Itchikawa and Baum[36] painted rabbits' ears with tar and could trace the development of carcinoma in some animals from the marked hyperplasia and hyperkeratosis of the epithelial cells, especially the cells of the hair follicles. The hyperplastic areas developed into follicula-epitheliomas and then there was further progression into definite carcinomas.

Since about 97 to 98 per cent of all cervical carcinomas are of the squamous-celled type, the study of excessive squamous-celled hyperplasia looms up as of the greatest importance.

D. Hyperplasia of Glands.—Several of the inflammatory cervices are characterized on section by a hyperplasia of the glands. The glands increase in number and may either be collected into patches or lie discrete. The increase varies, and in some the proliferating glands may be so numerous and with little intervening stroma as to suggest the formation of adenoma. The lining of the glands is mainly high columnar, which, however, can be changed to a low flattened type when the glands become cystic and are filled with much secretion.

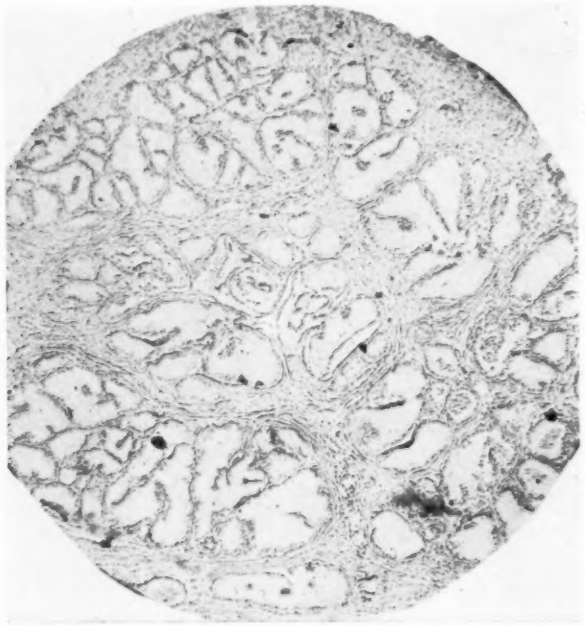

Fig. 9.—Cervix, patient aged thirty-four. Case of endocervicitis. Glandular hyperplasia simulating adenoma.

Many glands are noticed with papillomatous projections into the lumina. Occasionally an increase in number of lining layers may be noted. See Fig. 9. It shows one of several patches interspersed in the stroma. In this series there were 8 other such glandular hyperplasias, although they were lesser in degree.

Huggins[37] presents an illustration of this type in a polyp of the cervix and remarks that "the rather rare condition of adenocarcinoma occasionally starts in this type of growth." Stone's illustration[25] resembles Fig. 9, and he remarks: "There are glandular hyperplasias which lead to adenoma or adenocarcinoma." Adami and McCrae[38] recognize that there is a difference in degree only and not in kind between the inflammatory or irritative hyperplasia of glandular epithelium, the adenomas and finally the malignant glandular carcinomas.

Yeomans[39] discusses rectal adenomas. He believes that in their early stage there is a diffuse marked hypertrophy of the epithelial lining and quotes Ewing to that effect. He also mentions the view of Verse that irritation (bacterial, chemical, or mechanical) is a predisposing factor. He concludes, after remarking on the frequency of malignant changes of these adenomas: "Both clinically and by histologic study of the specimens, the transition from simple inflammatory hyperplasia to tumors pathologically cancerous can be traced through the stages of inflammation, gland cell hypertrophy and hyperplasia, and adenoma to definite adenocarcinoma. It is a logical inference that continuance of the irritative factors that induce the adenoma stimulate epithelial hyperplasia until it breaks through normal bounds and becomes malignant."

Senile Period.—This period includes the changes incident to "old age" and those due to sexual senility or the menopause. The cervix begins to atrophy and to undergo regressive and degenerative changes.

An interesting condition is seen in Fig. 10 (autopsy specimen, age fifty-three). In this case the cervix is undergoing senile degeneration

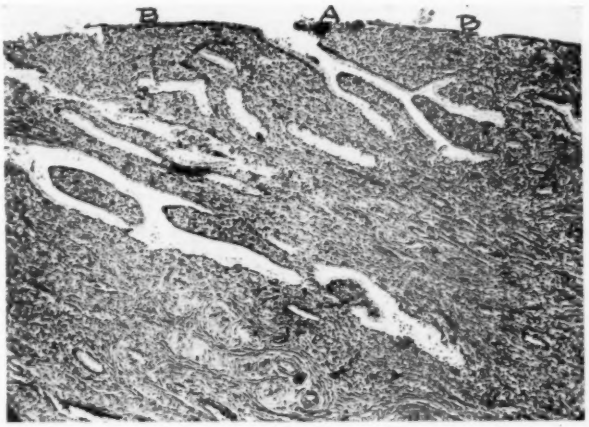

Fig. 10.—Cervix. patient aged fifty-three. Senile involution hyperplasia. In a field of senile degeneration is noticed a new hyperplastic condition of epidermization and gland formation. Note at *A* the new polygonal cells which are growing on the senile flat cuboidal lining, *B*. The newly formed glands are very evident. Some spots in the duct walls are still untouched by senility changes.

and the process is greatly varied in different parts. There is a marked hyperplasia of glands which is unusual for this age period. At one spot "*A*" the senile cuboidal lining layer merges with a patch of epidermization consisting of polygonal cells; in other words, there is a new formation of hyperplasia on the site of a senile degeneration.

Regressive hyperplasias are known to precede cancer, especially in the breast and prostate of seniles. According to Ewing[1] the chief condition predisposing to prostate cancer is chronic prostatitis, usually with hypertrophy. He makes the statement: "Whatever the nature of prostatic hypertrophy may be, it is clear that the influence of physiologic involution is concerned." He quotes other authorities who hold that 13.3 to 16.5 per cent of enlarged prostates after fifty years of age become malignant.

The skin in senile degeneration may show signs of old age and then be followed by marked hyperplasia which may proceed into the carcinomatous stage. Oertel[40] in routine examination of normal involuting breasts and prostates notes the frequent occurrence of carcinoid changes (potentially cancerous) and illustrates the growth of the proliferative atypical cells into duct lumina of these organs, and also to the outside of the duct wall. He describes the potentially malignant cells as follows: "These cells change their morphologic and tinctorial characters, assume appearances of altered differentiation with atypical shape and size and develop disturbed nuclear-plasma relations. Such abnormal cell types are also seen to undergo excessive hyperplasia." He finds these cell changes "not only in connection with general and otherwise typical glandular hyperplasia, but also in areas of gland reduction and collapse."

DISCUSSION

One is struck by the ready interchangeability between the two epithelia of the cervix throughout the different age periods. This occurs developmentally, physiologically, and pathologically. Far more frequent is the change of columnar into squamous epithelium, as has been sufficiently illustrated. The erosions, perhaps, give an example of the transformation of squamous epithelium of the portio to that of the columnar type.

Several writers have attested to the occurrence of metaplasias of the cylindrical epithelium of the endometrium. These have been shown to occur in menstruation, pregnancy, and after the menopause (Klein,[41] Mueller,[42] Moericke[43]). Hitschmann's[44] theory for this metaplastic occurrence in the endometrial epithelium is that the uterine mucosa retains the old embryologic characteristics of the müllerian ducts and has the power to transform into either type of epithelium. If one accepts this view, the cervix would naturally also possess this potentiality of epithelial differentiation.

Ontogenetically stratified squamous epithelium and cylindrical epithelium are closely related and both possess the natural ability to cover up exposed surfaces, although in the cervix the squamous epithelium is much more active in this respect. Squamous epithelium has greater powers of resistance than cylindrical, and this would explain the marked growth of the squamous layers in the erosions and in the so-called "metaplasias" of columnar epithelium. The stratification is laid down as a protection against the chronic irritant but unfortunately in many cases has the tendency to overstep bounds and to develop along atypical tendencies.

It would appear that there is a loss of balance between the two lining tissues of the cervix, as if the two epithelia were antagonistic and in opposition to one another. They are restrained, but there is a stronger tendency for the squamous cells to overrun the picture.

As shown above, even in the normal there is no fixed union of the two epithelia at the external os, but one can overstep into the other. This imbalance is greatly exaggerated following injury and inflammation, especially after labor, when in addition there is a strong inclination for the hyperplastic squamous epithelium to grow downward in the stroma. In other words, the cervix is a restless tissue and exceptionally liable to take on atypical growth due to the possession of two easily interchangeable epithelia.

Although none of the sections in this series can be classified as cancerous, yet a fair number are labelled "precancerous." There is much uncertainty as regards the meaning of this ill-used word. This is because of the lack of definite criteria that are characteristic histologically of this condition, and the fact that not all precancerous lesions go on to definite cancer. Because of this doubt the personal factor enters very largely in the matter of diagnosis of future cancer of the cervix from section examination, although clinically it is well recognized that there is a precancer stage.

Schauenstein,[45] Schottlander,[46] Ewing,[1] and Rubin[24] describe as characteristic of incipient carcinoma the following:

1. Irregular arrangement of cells.
2. Loss of cell boundary.
3. Abnormally close juxtaposition of cells.
4. Changes in chomatin network.
5. Changes in protoplasm toward stains (eosinophilia).

Findley[47] agrees with Ewing[1] who concludes that "when atypical hypertrophic and hyperchromatic cells are growing downward from the epidermis or fill enlarged gland alveoli the diagnosis of beginning carcinoma is justified." Frank[5] doubts the possibility of diagnosing early cancer in "conditions which, lacking as we do absolute histologic criteria of early malignancy, may as well prove to be harmless epithelial proliferation." He believes that a carcinoma is unmistakable, and insists that "while a specimen may be suspicious, in a given case we are dealing either with a cancer or not." He quotes Lubarsch as saying that cancer should be diagnosticated only "when one has found sure and clear criteria of destructive growth." Frank doubts Ewing's belief that we may be dealing with a condition "in the process of becoming cancer."

Healy[48] does not find the gross appearance of early carcinoma of the cervix typical and admits the difficulty of distinguishing chronic cystic and interstitial cervicitis with erosion from moderately developed or early infiltrating epidermoid carcinoma with ulceration. The weight of opinion, however, seems definitely to establish the conviction that there is an earlier predisposing phase of cancer, the precancer stage.

As previously mentioned, not all precancers turn into genuine cancers later. Various writers (Fluhmann,[27] L'Esperance,[49] Stone,[25] etc.) who believe in the evolutionary possibilities of development of cancer from the precancer stage, doubt whether all such precancers turn into malignancy. Some of the artificially produced tar cancers in animals do not develop into genuine cancers, although possessing a cancerous picture histologically. Borst suggests the term "carcinoid" rather than "precancerous," which ordinarily presumes a cancerous termination. In other words a carcinoid condition is potentially able to develop cancer, but does not necessarily do so.

Gynecologists are very much impressed with the frequency and virulence of cervical cancer and stress the necessity of early diagnosis. The majority believe in histologic examination of any suspicious tissue. Meyer and Kaufman[50] made biopsies of the portio in 146 cases, and found cancer in 26. In only 15 of this group had the clinical diagnosis been made. In 2 cases of this series the microscopic examination revealed cancer when it was not even suspected.

Immediate examination and repair of the large number of cervical lacerations occurring at labor is now urged. Some advise postpartum examinations with subsequent early repairs. The profession is being constantly advised on the signs of early cancer of the cervix. L'Esperance[49] suggests "systematic vaginal examination of women in the cancer zone, especially those who have borne children." All should view the cervix in the same light as Charlton[51] who aptly writes: "Let every chronically infected cervix be approached, not as a cervical catarrh, not as an hypertrophy, not as a laceration, but as the prologue of an epithelial drama whose curtain may be malignant death."

CONCLUSIONS

Microscopic examination has been made of 124 cervices, mostly cases of cervicitis (24 autopsy and 100 surgical). The following conclusions are presented:

1. The cervix is a restless organ with its tissue components continually in a state of imbalance.

2. There is a remarkable facility of interchangeability of the two lining epithelial types at all age periods.

3. From the very beginning, during the fetal period, there is no fixed union of the two epithelia at the external os but one can overstep into the other.

4. At labor the cervix is especially prone to develop an endocervicitis, due to the production of cervical lacerations.

5. Because of the restlessness of the cervical epithelia, endocervicitis is of great significance due to the metaplasias of the columnar lining and excessive downgrowth and thickening of the squamous epithelium which follow.

6. Many of the results of endocervicitis represent a precancerous stage, which need not necessarily go on to true cancer development. For these the term "carcinoid," suggested by Borst, is preferable.

7. In senility the regressive hyperplasias have to be considered in the light of a precancerous, or better, a dysontogenetic condition.

8. In the prophylaxis of cancer of the cervix, cervical lacerations should be quickly repaired. The local histologic examination in suspicious cases should be augmented by the clinical records. Surgery is

to be followed if the precancerous stage is greatly aggravated and true cancer seems imminent.

I wish to acknowledge my indebtedness to Professor Horst Oertel for his kindly interest and helpful suggestions.

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ETIOLOGIC FACTORS IN CARCINOMA OF THE CERVIX[1]

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DURING the last few years a great deal of information has been published concerning the structural classification, pathologic and clinical behavior, and the treatment of carcinoma of the cervix, by prominent clinicians,[1, 2, 3, 4, 5] but, with relatively few exceptions, the etiology of the disease has been carefully avoided.

Cullen[6] reviewed the various conspicuous theories of malignancy (heredity, trauma, Cohnheim's cell inclusion, Ribbert, Virchow, parasitic) and finally agreed with Hannseman and Hauser that cancer is primarily a disease of the epithelium, but emphasized our ignorance of the causes of cell alteration. Such authorities as Bloodgood,[8] Mallory,[9] Councilman[10] and Schiller[11] have agreed as to the uncertainty of the origin of cancer. Ewing[7] suggests that there are different factors in the different types of malignancy found in various anatomic locations.

Many writers have noted cancer of the cervix to be a disease of the poor and ill-nourished classes. Theilhaber believes that cancer develops in poorly nourished organs and cites as a factor that the menstrual life of the poorer classes averages five to six years less than that of better constituted women.

Frazer[22] points out as factors in the causation of cancer: Chronic Irritation coupled with a Predisposition to the disease. Loeb[23] and Slye[24] believe that any inherited resistance to the development of cancer can be overwhelmed by a chronic irritant of sufficient strength.

Bailey[25] suggests as a basic cause of cancer of the cervix that there are many initial causal factors concerned in the production of an intermediate causal factor which is constant. This intermediate causal factor is the inflammatory exudate in contact with the epithelium.

Shaw[26] states that there is no specific substance which alone is cancerogenic; the specificity lies in the physicochemical complex of viscosity, insolubility in the tissue fluids, and toxicity.

Stone,[12] Graves,[13] Healy[14] and others have pointed out as a factor, the trauma of parturition with its resulting laceration of the cervix, ectropion and erosions. In the statistics of Healy,[14] Farrar,[15] Leipman, Kolblouch and Theilhaber, in whose series nulliparae represent only 2.5, 4.0, 1.77, 4.6, and 2.9 per cent respectively and the number of patients with pregnancies varied between 92 per cent and 98 per cent, this factor is shown to be relatively constant.

However, since many women of the poorer classes, having multiple pregnancies, do not develop cancer of the cervix, other factors must be involved. Howitz,[17] in reviewing cervix cases at The Mayo Clinic, has reported that in spite of their noted fertility and longevity, the disease was only one-fourth as frequent in Jewesses as in Gentile women. L'Esperance[20] has suggested the possibility of the failure of younger Jewish women to observe the Mosaic Laws as a factor in the increasing

[1]Read at the Obstetric and Gynecologic Section of the New York Academy of Medicine, May 27, 1930.

evidence of cancer of the cervix among Jewish women, and work is now being done by her from this angle. Reel[16] and many others have stated the necessity of cleaning up erosions and low-grade infections as prophylaxis against cervical cancer. Smith, Smithwick and Rogers[18] in 1928 reported that of 550 cases of cancer of the cervix only 2 had had trachelectomies performed and not one had been treated with the cautery. Also of 1150 cervicitis cases treated with a cautery between the years 1914 and 1923, not one had developed cancer of the cervix at the time of this publication. Surely, then, there must be other factors than the lacerated cervix and associated ectropion of mucosa, as induced by the trauma of parturition. Adair[19] suggests that one must look for chemical and bacterial, as well as mechanical, factors.

With these factors in mind, a series of cases of known carcinoma of the cervix has been compared with a practically equal number of patients who have escaped the disease, in the attempt to discover wherein the two series differ and with the hope of finding possible etiologic factors.

Because of the constant high percentage of women who have had pregnancies, in all the reported cervical cancer series, only patients that had had two or more pregnancies and had reached the age of cancer incidence have been selected for the control group. Knowing cancer of the cervix to be a disease of the poor, all of the control group were selected from patients in the clinics and wards of Memorial and other hospitals. The statistics were obtained by personally interviewing each of the 226 cancer patients and the 202 patients of the control group. The cancer patients were taken from the Gynecological Service of Memorial Hospital.

TABLE I. CLASSIFICATION OF CANCER SERIES AS TO MARRIAGE AND PREGNANCIES

	NUMBER	PER CENT OF TOTAL
Total number of cases	226	100.0
Married	222	98.2
Single	4	1.8
Married but no pregnancies	12	5.3
Pregnancies	210	92.8

This shows the classification of the cancer series with the low percentage (1.8 per cent) of nulliparous women and the high percentage (92.8 per cent) of women having pregnancies as a constant factor in the selection of control patients.

TABLE II. CLASSIFICATION OF CONTROL CASES

LESIONS	NUMBER
Breast	58
Fibroids	54
Pregnancy	52
Stomach	3
Ovarian	6
Vulva	3
Senile vaginitis	6
Endometritis menopause	19
Lymphosarcoma skin	1
Total	202

This is the classification as to diagnosis of the control patients. It is to be noted as a possible weakness in the selection of controls that 52 were maternity patients in wards of New York Lying-In Hospital; a weakness because practically no time elapsed between the last delivery and the time of interviewing the patient, hence, theoretically, not time for cancer to develop. However, all of these 52 cases were between thirty-six and forty-six years of age (37 being under forty years, 15 over forty years) and had had more than two children, and eight years or more had elapsed since their first delivery.

TABLE III. COMPARISON OF TWO SERIES AS TO NATIONALITY

	CARCINOMA		CONTROL	
	NUMBER	PER CENT	NUMBER	PER CENT
Black	20	8.8	31	15.3
White	206	91.1	171	84.6
German	20	8.8	17	8.4
Italian	74	32.7	30	14.8
Jewish	15	6.6	33	16.3
Greek	2	0.8	0	0.
Irish	45	19.4	52	25.7
Polish	8	3.5	3	1.4
Others	42	18.5	36	17.8
Total cases	226		202	

The comparison of the two series as to nationality is of interest because it shows Italians to make up about a third of the cancer group. While cancer of the cervix is known to be prevalent among Italians, their relatively large proportion in this series may be misleading because of Memorial Hospital's large Italian clientele.

TABLE IV. COMPARISON OF CANCER AND CONTROL SERIES AS TO AVERAGE AGE, NUMBER OF PREGNANCIES, AND TIME SINCE LAST PREGNANCY

	CARCINOMA		CONTROL	
	NUMBER	PER CENT	NUMBER	PER CENT
Total	226 210 (Preg.)		202	
Average age	46.0 yr.		44.2 yr.	
Youngest	26 yr.		36 yr.	
Oldest	66 yr.		69 yr.	
Under 40 years	50	22.1	52	25.7
Average number pregnancies	3.9		3.4	
Average time since last pregnancy	17.5 yr.		16.5 yr.	
Last pregnancy within five years	17	8	52	25.7
Last pregnancy within ten years	53	20.4	57	28.4

While the average age of the control group at the time interviewed is forty-four and two-tenths years as opposed to forty-six years for the cancer group (Pack's[21] average age for all cases of cancer of the cervix at Memorial Hospital is forty-eight years), the range of ages was higher in the control group and excluding the 52 maternity patients, the average age of the remaining controls was forty-seven and two-tenths years. The number of patients under forty years of

age and the average number of pregnancies for each patient shows a favorable comparison in the two groups. The average time since the last pregnancy is about equal including all cases. Excluding the 52 maternity cases this average time for the remaining control patients is twenty-three years. The only control patients having the last pregnancy within five years were the 52 maternity patients. Only 5 of the remainder of the controls had their last pregnancy within ten years, giving a total of 57 patients which compared satisfactorily with the cancer group.

Thus it would seem that the selection of these patients as a comparison group is justified.

TABLE V. COMPARISON OF TYPES OF MENSTRUATION

MENSTRUATION	CARCINOMA		CONTROL	
	NUMBER	PER CENT	NUMBER	PER CENT
Age of onset (average)	13.7 yr.		14 yr.	
Average duration	4.7 days		4.8 days	
Irregularity	28	12.3	32	15.8
Dysmenorrhea	130	57.5	81	40.1
Dysmenorrhea after marriage	12	5.3	9	4.3

This is a comparison of types of menstruation. There is practically no marked variation between the two series. The group having dysmenorrhea at any time show the only noticeable difference and because of the difficulty of discounting the individual varieties of each patient's estimation of her dysmenorrhea this slight difference is discarded in concluding that menstruation is not a factor in carcinoma of the cervix. The time since menopause has not been considered, as a great many of the carcinoma group had not appreciated any onset of menopause. This is possibly a field for further investigation.

TABLE VI. COMPARISON AS TO PREGNANCIES, MARRIAGE AGE, AND INTERVAL BETWEEN MARRIAGE AND CHILD BIRTH

	CARCINOMA		CONTROL	
	NUMBER	PER CENT	NUMBER	PER CENT
Average number of pregnancies	3.9		3.4	
One pregnancy only	40	19.0	0	0
Three or more pregnancies	138	65.7	131	64.8
Miscarriages	43	20.4	29	14.3
Average marriage age	20 yr.		21.4 yr.	
Average time before first baby	2.4 yr.		1.4 yr.	
First baby within one year after marriage	6	2.3	97	48.0
First baby within two years after marriage	70	33.3	175	86.6
First baby after two years	140	66.6	27	13.3

The average number of pregnancies and the average number of patients having three or more pregnancies show a practical equality. Of course, there were no patients, having one pregnancy only, in the control group. The number of patients having miscarriages seems

surprisingly small in both groups, but were the figures obtained. No information was sought as to percentages of induced abortions. This would possibly be of interest for its bearing on instrumentation of the cervix. The average marriage age was slightly higher for the controls. The average time between marriage and the first delivery shows a significant difference (two and four-tenths years for the cancer group as against one and four-tenths for the control). This leads to further speculation as to the use of contraceptives in spite of the belief that birth control is not practiced among the poor. Especially is it of importance when we consider that 66.6 per cent of the cancer group had their first delivery more than two years after marriage, as opposed to only 13.3 per cent for the controls. This is taken as the first possible factor in carcinoma of the cervix.

TABLE VII

TYPE DOUCHE	CARCINOMA		CONTROL	
	NUMBER	PER CENT	NUMBER	PER CENT
Lysol	103	49.1	37	18.1
No douche	41	19.5	58	28.7
Salt	20	9.9	18	8.9
Boric	18	8.5	27	13.4
Water	15	7.1	49	24.2
Soda bicarb.	8	3.8	7	3.4
Peroxide	1		0	
Alum	2	less	2	less
Potas. permang.	2	than	2	than
Luko	0	1%	1	1%
Mucol	0		1	

It is of some interest to note that only two-thirds as many cancer patients as controls used no douches at all. No attempt has been made to determine the frequency of douching nor the strength of the solution used. All types of douches taken are those used before the onset of symptoms.

Striking is the increase in the number of cancer patients using Lysol douches over those of the control group. Lysol is a saponified product of coal-tar containing cresol, which in turn comes from beech-tar by distillation. Since 1914, when Yamagiwa[27] and Itchikawa succeeded in producing papillomas in rabbits' ears by repeated applications of tar, we have found the tars and oils in universal employment in the experimental production of cancer. Woglom[28] quotes industrial evidence that creosote oil produces cancer. De Jong,[29] Meyer and Martineau report squamous carcinoma developing on an eczematous area which had been painted daily for several years with coal-tar to allay the itching. As eczema is not known to be followed by cancer, they believed it reasonable to blame the tar for the production of the cancer. On the sole basis of the comparison between the cancer patients and controls, the use of Lysol douches is taken as the second possible etiologic factor in carcinoma of the cervix.

There was a moderate increase for the cancer group over the controls in the number of patients having one or more instrumental deliveries, but in this age of so-called prophylactic forceps in primiparae, this difference can hardly be given much weight. Those patients having, however, more than one instrumental delivery show that there were nearly five times as many in the cancer as in the control group. This is taken as the third possible factor.

TABLE VIII. COMPARISON OF CANCER AND CONTROL GROUP AS TO INSTRUMENTAL DELIVERIES, DRY LABORS, CERVICITIS, AND TREATMENT

	CARCINOMA		CONTROL	
	NUMBER	PER CENT	NUMBER	PER CENT
Instrumental delivery	63	30	48	23.7
More than 1 instrumental delivery	21	10	5	2.4
Dry labors	128	60.9	41	20.3
More than 1 dry labor	44	20.9	9	4.4
Both instrumental and dry labor	39	18.5	8	3.9
Leucorrhea	59	28	81	40
Cases receiving any treatment	3	1.4	63	32
Per cent cases entitled that received treatment		5		77.7
Trachelectomy	3		5	
Cautery	0		18	
Clinic or doctor	0		40	

TABLE IX. ETIOLOGICAL FACTORS IN CARCINOMA OF CERVIX

1. First baby more than 2 years after marriage.
2. Use of lysol douches.
3. More than one instrumental delivery.
4. Dry labor.
5. Untreated cervical lesion as manifested by leucorrhea.

	CARCINOMA		CONTROL	
	NUMBER	PER CENT	NUMBER	PER CENT
All factors present	3	1.3	0	0
4 factors present	8	3.5	0	0
3 factors present	45	19.5	4	1.9
2 factors present	105	46.4	23	11.3
1 factor present	42	18.6	41	20.7
Cases with one or more	203	89.8	68	33.6
No factors present	23	10.1	134	66.2
2 or more factors present	161	71.2	27	13.3

Dry labors show an astounding difference (60.9 per cent for the cancer group to only 20.3 per cent for the control). This is accentuated by 20.9 per cent of the cancer group having more than one dry labor as against only 4.4 per cent of the controls. Therefore, dry labor is taken as the fourth possible factor.

Leucorrhea, taken as the indication of cervicitis, erosion and probably laceration, occurred in more controls (40 per cent) than in patients of the cancer group (28 per cent). This might mean that the cancer group were too careless of body hygiene to recognize the leucorrhea, though the fact that more cancer patients than controls used douches would seem to dispute this supposition. It is of great

significance, however, that of patients requiring treatment for leucorrhea, 77.7 per cent of the controls received it as opposed to only 5.0 per cent of the cancer group. Therefore, untreated cervical lesions as manifested by leucorrhea is taken as the fifth possible factor.

It is of interest that the control and cancer groups are about equal in the number of patients having present any one of these possible factors only, but with the increase of the number of these factors present, the inequality in percentage comparison progressively increases. Of the 23 cancer patients having no factor present the 4 single women and the 12 married but never pregnant women should be further discounted because these 16 women could be considered as being exposed to only two of these factors (i.e., lysol douches and untreated cervical lesions) although the first factor must be considered with the 12 married patients. Eleven of the 23 cancer patients with none of these factors present are of the group of 16 that have had no pregnancies.

CONCLUSIONS

1. Parturition with its resulting damage to the cervix is a generally accepted etiologic factor in cancer of the cervix. With the majority of cancer patients proving to be multiparous, this factor increases in importance with the number of pregnancies.

2. The incidence of the disease is known to be higher in the poorer classes.

3. By comparison of a series of cancer patients with a control series with the two known factors constant in each series, there are apparently five additional possible factors.

   a. Length of time between marriage and first delivery (more than two years being selected for these statistics) with the suggestion of a possible field for investigation as to contraceptives used.
   b. Use of lysol douches.
   c. More than one instrumental delivery.
   d. Dry labor.
   e. Untreated cervical lesions as manifested by leucorrhea.

4. One of these five possible factors only was not present more often in cancer patients than in the control group but, with the incidence of two or more of the factors present, the inequality in percentages of each group total progressively increased with the increase in number of factors. It can certainly be considered that when two or more of these additional factors are present with the known factors of parturition and poverty, the incidence of cancer of the cervix is increased.

5. Menstruation is not shown to be a factor in carcinoma of the cervix.

6. Possible factors suggested as fields for further investigation are:
   a. Incidence of induced abortions with special reference to instrumentation.
   b. Contraceptives: types and duration of use.
   c. Duration of labor.
   d. Frequency of intercourse.
   e. Observance of Mosaic Laws.

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Results with Ried's irradiated salve (Metuvitsalbe) in infectious skin conditions led the author to investigate the effects of irradiated fat in gynecologic conditions. Masses of irradiated fat in the form of globules and bougies for vaginal use were produced. In 26 cases of vaginitis in patients of all ages, discharge and burning disappeared in two to three weeks. Erosions of the cervix healed, but in cases of adnexal disease there was no effect. Symptomatically the patients improved, especially where there was annoying discharge.

Frank Spielman.

NEPHRITIS IN PREGNANCY

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(From the Medical Service of the Chicago Lying-In Hospital)*

NEPHRITIS in pregnancy, although not a frequent complicating occurrence, is a very serious one. During pregnancy the renal burden, as well as that of the heart,[1] is increased and the whole body economy is disturbed. Impaired renal efficiency becomes inadequate more easily in pregnancy because of this increased burden. The neurovascular system shows evidence of increased instability,[2] the fat, carbohydrate, and protein metabolism is altered and the whole endocrine system is disturbed. A mild acidosis occurs in normal pregnancy, particularly during the last weeks.[3, 4] Anemia is frequently notable and at times is severe.[5, 6] All these factors adversely affect the processes of renal repair and rehabilitation during pregnancy and probably contribute in an indirect fashion to the etiology of such renal disturbances.

Renal disease in pregnancy is of several types. The classification of these types is essential for a proper conception of the problems of etiology, pathogenesis, symptomatology, therapy, and prognosis. A pathologic classification is both difficult and unsatisfactory. An etiologic classification is at present impossible, as the exact etiology of these vascular and renal disturbances is still shrouded in doubt. They all represent tissue reactions to an intoxication, but the source of this intoxication is uncertain. Separation of the acute and chronic cases of nephritis in pregnancy into two groups aids in establishing the prognosis.[7] The suddenness of onset is one of several criteria of the nature of the causative intoxication. Much confusion exists regarding the best means of classifying the renal injury, especially regarding the use of the terms nephritis and nephrosis.[8, 9, 10, 11, 12] These terms we shall carefully avoid, as their present status and meaning are interpreted too variously. To include renal injury in pregnancy under the heading of "toxemias of pregnancy" is grossly inaccurate; the intoxication in renal disease here as elsewhere affects the tissues primarily and often alters the blood but little. There is almost no conclusive evidence that the intoxication is one of the blood, as implied by the term "toxemia."

A recently popular term in the classification of renal injury in pregnancy is "low reserve kidney."[13] As used, the meaning of this phrase is grossly perverted[12] to mean a mild late intoxication in pregnancy with only slight arterial hypertension, moderate albuminuria, and

*The work was aided by a grant from the Mothers' Aid Society of the Hospital.

prompt recovery. An actually reduced renal reserve resulting from previous renal disease manifests itself far earlier in pregnancy and is associated with persistent and often excessive hypertension which is aggravated and often permanently increased by the intoxication and increased burden of the pregnancy. What has been called the "low reserve kidney" is better named the "syndrome of tissue and renal fatigue in pregnancy."

A clinical view of the types of hypertension and nephritis as occurring in pregnant women permits of their classification into four groups.[14] These groups may be listed, for convenience' sake, as follows: A, albuminuria of pregnancy (renal fatigue syndrome); B, eclamptic and pre-eclamptic intoxication; C, nephritis and hypertension in pregnancy in patients in whom preexistent renal and/or vascular disease has reduced the renal reserve, with exacerbation of these processes of pregnancy, and D, nephritis and hypertension with definite complications, such as thyrotoxicosis, cardiac disease, acute infections or obstetric difficulties. The last group, of course, overlaps the other three and is listed separately only because of the necessity of individualization in therapy. This grouping of cases has been employed by the medical service at the Chicago Lying-In Hospital for the last several years and has proved its practical clinical value in the evaluation of the individual prognosis and determination of the mode of therapeutic attack.

REPORT OF CASES

In the last three years over 60 cases of nephritis in pregnancy have been observed and studied by the medical service at the Chicago Lying-In Hospital, from which the following data have been obtained. Of these 60, 5 were unsuitable for analytic study because of an insufficient duration of stay. The 55 cases which constitute a basis for the present report are derived from both the private and ward services. The majority have been followed up-to-date, either by direct study or by questionnaire.

The clearest presentation of the facts observed can be made by presenting the data in tabular form. (See Table I.)

It is notable that considerable variation exists in the characteristics observed, as these tabulated cases represent a mixed collection of various forms of renal disturbance. Table I, however, serves as a basis of comparison for the data observed in the individual groups. The most uniform observation is that of arterial hypertension in association with nephritis, this being noted in 87 per cent of all the cases. The arterial hypertonia must not be considered a result of the renal disturbance, but undoubtedly arises as a result of direct vascular irritation by the same factors being causative of the renal injury.[14] Analysis of the methods by which pregnancy was terminated reveals

TABLE I

FINDINGS IN ALL CASES:		NO.	PER CENT
Total number		55	
Average age		26.8	
Maximum age		42	
Minimum age		16	
Average number of pregnancies		2.4	
Maximum number of pregnancies		10	
Number of primiparas		32	60
Symptoms:			
Onset of symptoms occurred at 9 mo.		10	18
Onset of symptoms occurred at 8 mo.		15	27
Onset of symptoms occurred at 7 mo.		15	27
Onset of symptoms occurred at 6 mo.		8	14
Onset of symptoms occurred at 5 mo.		2	3
Onset of symptoms occurred at 4 mo.		3	5
Onset of symptoms occurred at 3 mo.		2	3
Onset of symptoms abrupt in		30	54
Onset of symptoms insidious in		25	46
Earliest Symptoms Noted:			
Albuminuria		20	36
Edema		16	29
Cephalalgia		13	23
Visual disturbances		3	5
Coma		1	2
Asthenia		1	2
Asymptomatic hypertension		10	18
Icterus		1	2
Hypertension occurred in		48	87
Average arterial tension	177/113		
Maximum arterial tension	256/180		
Associated Complications Observed:			
Cardiac decompensation		3	5
Acute infective nephritis		1	2
Thyrotoxicosis		1	2
Impaired renal reserve (functional tests)		41	74
Fever		6	11
Syphilis		3	5
Marked anemia		3	5
Arsenical poisoning (arsphenamine)		1	2
Recurrent eclampsia		1	2
Convulsions		4	7
Hematuria (gross)		2	4
Delivery:			
Delivered at 9 mo.		21	38
Delivered at 8 mo.		20	36
Delivered at 7 mo.		8	14
Delivered at 6 mo.		2	3
Aborted at 5 mo.		1	2
Aborted at 4 mo.		1	2
Aborted at 3 mo.		2	3
Delivered spontaneously		25	45
Delivered by cesarean section		8	14
Delivered by vaginal section		4	6
Delivery induced by gauze		6	11
Delivery induced by oleum ricini and quinine		5	9
Delivery induced by bag		2	3
Delivered by version		1	2
Aborted (surgically)		4	7
Deaths:		2	4

that approximately half delivered spontaneously; only in approximately 10 per cent of the cases was delivery prior to fetal viability necessary. A maternal mortality of only 4 per cent may be considered as evidence confirming the wisdom of the methods of therapy chosen.

Of physiologic rather than pathologic interest is the observation that in 85 per cent of these patients a notable postpartum rise in arterial tension occurred coincidently with the onset of lactation. This rise is associated with a transient diminution of the circulating blood calcium[16] and occurs in both those patients with normal and with raised arterial tension. The calcium content of the blood is probably of no great significance in the etiology of abnormally elevated arterial tonus but is a factor in the control of physiologic variation in the arterial tension.[16]

Of greater significance and interest are the analyses of the specific clinical groups of nephritis in pregnancy as observed in this series.

TABLE II

GROUP A. SYNDROME OF RENAL FATIGUE IN PREGNANCY	NO.	PER CENT
Total number of cases	21	
Average age	26.4	
Average number of pregnancies	1.8	
Maximum number of pregnancies	5	
Number of primipara	11	52
Symptoms:		
Onset occurred on the average at 8 mo.		
Onset was abrupt in	14	68
Onset was insidious in	7	35
Edema most conspicuous symptom in	8	40
Albuminuria most conspicuous symptom in	9	50
Arterial hypertension most conspicuous symptom in	3	14
Asthenia most conspicuous symptom in	1	5
Average arterial tension 153/97		
Associated Complications Observed:		
Residual nephritis on discharge	3	14
Fetal death	4	20
Syphilis	2	10
Thyrotoxicosis	1	5
Infection	3	14
Marked anemia	3	14
Low renal reserve (on functional tests)	10	50
Delivery: Delivered on average at 8.6 mo.		
Spontaneous labor	14	66
Labor induced	3	14
Cesarean section	4	20
Deaths:	0	0
Late Results: From 6 mo. to 3 years.		
In good condition	15	71
In fair condition	1	5
In poor condition	0	0
In bad condition	0	0
Unknown	5	24

Group A. The Syndrome of Renal Fatigue in Pregnancy.—This group, often erroneously designated as "the low reserve kidney," represents approximately 40 per cent of the total number of nephritides in pregnancy. Other clinics report an incidence of 35 per cent.[12] (See Table II.) The most notable characteristics of this group are revealed in the character of the onset of symptoms, the relatively low average level of the arterial tension, the late appearance of the disturbance, the late average date of delivery, the absence of any maternal deaths, and the excellent late results from six months to three years after the pregnancy.

The average onset of symptoms was at eight months, and the onset was abrupt in 68 per cent of cases. The most frequent clinical findings were albuminuria, moderate edema, moderate elevation of the arterial tension. In half the patients a reduction of the renal reserve was

TABLE III

GROUP B. ECLAMPTIC INTOXICATION	NO.	PER CENT
Total number of cases	14	
Average age	26	
Average number of pregnancies	3.2	
Maximum number of pregnancies	10	
Number of primipara	**8**	**57**
Symptoms:		
Onset occurred on the average at 7.5 mo.		
Onset was abrupt in	13	92
Onset was insidious in	1	7
Albuminuria was most conspicuous symptom in	4	28
Profound intoxication was most conspicuous symptom in	4	28
Edema was most conspicuous symptom in	1	7
Coma was most conspicuous symptom in	1	7
Arterial hypertension was most conspicuous symptom in	3	21
Icterus was most conspicuous symptom in	1	7
Average arterial tension 185/115		
Associated Complicating Factors:		
Fetal deaths	6	43
Appendiceal abscess	1	7
Left hospital in poor condition	5	35
Low renal reserve (on functional tests)	11	80
Delivery: Delivered on average at 8 mo.		
Spontaneous labor	5	35
Induced labor	3	21
Aborted	2	14
Cesarean section	2	14
Vaginal section	2	14
Deaths: From postpartum convulsion at 7 mo.	1	7
Late Results: From 6 mo. to 3 years later.		
In good condition	6	43
In fair condition	0	0
In poor condition	0	0
In bad condition	1	7
Unknown	7	50

manifest by a failure of the kidneys to secrete urine of adequate specific gravity following deprivation of water for from fourteen to eighteen hours.[15, 17] The ability of the kidneys to concentrate the urine adequately may be taken as the most significant single criterion of the renal functional reserve.[15, 18, 19] These patients were delivered on an average at 8.6 months of gestation, or very close to full term. Characteristic of the group is the excellent repair and return to full normal health after the termination of pregnancy. Of the patients whom we were able to follow for a considerable period of time, 94 per cent were in good health, 6 per cent in fair health, and no known instances of poor or bad health were observed. This evidence of an excellent prognosis is in sharp contrast with the observations in Group C.

Group B. Eclamptic or Preeclamptic Intoxication.—Here an entirely different clinical picture is manifest. (See Table III.) An abrupt, almost explosive, onset of symptoms occurred in 92 per cent of these preeclamptic patients, who comprise approximately 30 per cent of these women with nephritis in prgnancy. The intoxication is more profound than in either of the other groups; edema and albuminuria become relatively less significant. Marked icterus, evidencing hepatic injury, is observed here, but not in Group A or Group C. The onset of symptoms occurs moderately early, at seven and a half months of pregnancy on the average, in contrast with eight months in Group A. The average arterial tension for the group is considerably higher and particularly is the marked diastolic hypertonia of interest. The incidence of primipara is almost uniform throughout the three groups.

Delivery was earlier on the average in these patients than in those suffering from the syndrome of renal fatigue in pregnancy and surgical interference was far more frequent and necessary. One death occurred in this group from postpartum convulsions of an eclampsia occurring at seven months gestation. The follow-up studies reveal that, although the immediate prognosis is notoriously precarious, the late prognosis is essentially good, and little evidence of permanent residual injury is noted. The repair following this profound intoxication is relatively slow as revealed by the fact that a third of these patients left the hospital in poor condition. During the intoxication a reduction of the renal ability to concentrate the urine adequately was noted in 80 per cent of the patients.

The clinical syndrome of eclamptic or preeclamptic intoxication in pregnancy may be briefly characterized as follows: An acute, sudden, and abrupt profound intoxication of the entire body coming on usually in the midst of the third trimester of pregnancy, associated with marked hepatic, vascular, and cerebral, as well as renal injury, having a relatively poor immediate but good late prognosis. The intoxication

is of unknown chemical nature and of uncertain source, but is clearly attributable to some aspect of the pregnant state.

Group C. Nephritis in Pregnancy With Preexisting Vascular and / or Renal Disease.—In many respects this is the most interesting of all the groups, as clinically, pathologically, etiologically and regarding the prognosis it represents the superimposition of two distinct disease processes. Attempts have been made to place hypertensive arterial disease as a subdivision of nephritis.[12] Such a classification is absurd,[15] as arterial disease is a clearly individual clinical entity and, although it is frequently associated with renal disease, is rarely dependent upon the renal disturbance. This group of cases constitute approximately 40 per cent of the total number of cases of nephritis in pregnancy in this series. Other reports[12] place the incidence as low as 25 per cent of all gestation intoxications.

TABLE IV

GROUP C. WITH PREEXISTING VASCULAR AND/OR RENAL DISEASE	NO.	PER CENT
Total number of cases	20	40
Average age	28.4	
Average number of pregnancies	3.2	
Maximum number of pregnancies	10	
Number of primipara	11	55
Symptoms:		
Onset occurred on the average at 5.8 mo.		
Onset was abrupt in	4	20
Onset was insidious in	16	80
Symptoms first noted were: Cephalalgia	5	25
Symptoms first noted were: Albuminuria	5	25
Symptoms first noted were: Arterial hypertension	5	25
Symptoms first noted were: Edema	3	15
Symptoms first noted were: Visual disturbances	2	10
Average arterial tension 194/148		
Associated Complicating Factors:		
Reduced renal reserve (functional tests)	18	90
Marked anemia	3	15
Thyrotoxicosis	1	5
Cardiac decompensation	1	5
Fetal death	12	60
Discharged from hospital in poor condition	14	70
Delivery: Delivered on average at 7 mo.		
Spontaneous labor	8	40
Induced labor	6	30
Cesarean section	3	15
Aborted	3	15
Deaths:		
Cardiac failure postpartum at 8 mo.	1	5
Late Results: From 6 mo. to 3 years later.		
In good condition	0	0
In fair condition	3	15
In poor condition	9	45
In bad condition (1 died since)	5	25
Unknown	3	15

The clinical syndrome of preexisting renal and/or vascular disease with superimposed pregnancy is characteristic and clearly defined. (See Table IV.) In contrast with the other groups the onset of subjective and objective symptoms occurs much earlier in the course of pregnancy, averaging five and eight-tenths months. The onset is insidious and arterial hypertension is most pronounced. In the present series the average arterial tension of patients of this group was 194/148; a remarkable average diastolic hypertonia. However, the relative rise in arterial tension during the course of pregnancy is no greater than in the other forms of intoxication with nephritis. Early delivery is the rule, the average delivery being at seven months gestation. About one-third of the deliveries were by surgical intervention.

An essential characteristic of the group is the frequency with which the renal functional reserve is impaired (in 90 per cent), and the failure of these patients to show much improvement in the vascular and renal disturbances after termination of pregnancy. The phenolsulphonephthalein test of renal function, although frequently altered at the end of pregnancy[20] is of relatively little value as an index to the *reserve* of renal efficiency. At the end of the puerperium the arterial tension and urinary findings are not normal.[21] Nor is much rehabilitation to be expected later, as shown by the follow-up studies which revealed that up to three years after their hospital observation 80 per cent of followed cases were in poor or bad condition. Each succeeding pregnancy leads to further renal degeneration and further exacerbation of the vascular disease, with increasing evidence of arteriosclerosis.[27]

Cardiac inadequacy and severe anemia[28] are to be dreaded in these patients either during the exacerbation in pregnancy or following it. Every effort must be made to spare the heart. The fetal mortality of 60 per cent is the highest of any of the forms of nephritis in pregnancy. Retinitis is found here most frequently, although it also occurs in the syndrome of renal fatigue (Group A).[22] Retinitis is said not to occur in true eclampsia or preeclampsia.[23] The retinitis is chiefly vascular[24] and rarely is impairment of vision permanent[25] unless retinal hemorrhages occur.

Group D. Nephritis in Pregnancy With Additional Complications.—The patients in this group of course overlap into the other divisions. Seven cases of the 55 fall into this classification, of which 6 were also of Group A, and one also of Group C. The complicating factors were: active syphilis twice, acute puerperal infections twice, cardiac exhaustion once, pyelitis once, and severe anemia once. Arsenical intoxication from overly enthusiastic antiluetic therapy was responsible, at least in part, for one instance of nephritis in pregnancy in the present series. Arsenical and mercurial preparations are two-edged swords[29]

and, as they injure primarily the liver and kidneys,[30] are particularly dangerous during gestation.

In this group the problem of diagnosis, therapy, and prognosis are, of course, purely individual and do not concern the main theme of the report. Anuria is most unusual.[31]

COMMENT

To discuss adequately the multiple problems and aspects of the field of renal and vascular disease both in or independent of pregnancy is beyond the scope of the present report. It is desirable, however, that several specific aspects be dealt with briefly. Of particular significance here are the etiologic factors productive of nephritis in pregnancy, the pathogenesis of the changes therein, the logical foundation for intelligent therapy, and the evaluation of the prognosis.

The etiology of the intoxication of pregnancy is still grossly obscure, and has not yet emerged from the phase of nebulous theorizing. Of the theories advanced the most probable are[12]: (1) Intoxication from fetal elements; (2) from fetal metabolites; (3) placental products; (4) biologic (anaphylactic) reactions; (5) physical chemical changes resulting from altered maternal metabolism, and (6) uremic intoxication from renal decompensation. The scientific evidence advanced in promotion of these various conceptions is not thoroughly convincing.[65] Implication of the placenta as the origin of much of the intoxication has been based upon most logical evidence.[32, 33, 34, 35] Extraneous factors, such as weather and the dietary changes of the war, affect the incidence of the eclamptic form of intoxication but are undoubtedly merely contributory rather than primary etiologic factors.[12] The chemical nature of the intoxicating substance or substances is wholly unknown.

The tissues of the whole body are involved in these intoxications; there is no evidence of a purely local renal disturbance in any instance. These intoxications cause widespread changes here, as in nephritis unassociated with pregnancy. These changes are in part, at least, probably active as protective mechanisms. We have learned to think of edema with nephritis rather than of nephritis causing edema.[15, 36, 37, 38] Even more recent work has indicated that albuminuria may be an active protective mechanism,[39, 40, 41] similar to the protection against excessive hyperglycemia afforded by the glycosuria in diabetes mellitus. Hypertension, or increased arteriolar tonicity,[15] is perhaps the best guide to the severity of these intoxications, both as regards the height of the diastolic arterial tension and also the abruptness of such elevation. Hypertensive arterial disturbances are the result of vascular irritation or intoxication, and do not imply any notable change in the circulating blood. Hence the inaccuracy of the term "toxemia" as applied to these intoxications of pregnancy.

The renal tissues are injured synchronously with the changes throughout the body. The only direct evidence of such renal injury is the observation that the renal functional efficiency is so frequently impaired. Albuminuria per se is not a certain criterion of renal injury, nor is the degree of albuminuria an adequate guide to the degree of renal damage.[15] It has been shown that the majority of the protein in the urine in nephritic albuminuria is of hepatic origin[40] and not infrequently results from metabolic changes.[42, 43] Adequate concentration of the urine under conditions of stress, such as during or following water deprivation, is however a purely renal matter and the frequent failure of the kidneys of these patients to concentrate the urine properly under such conditions of increased effort is convincing proof of direct renal inadequacy.[5, 6, 15]

Anemia in pregnancy is usual. In the absence of severe nephrotoxic intoxication recovery from such anemia is relatively prompt and complete.[44] In the instances cited in Group C, where pregnancy caused an exacerbation of preexisting renal and/or vascular disease, such prompt improvement does not occur. Energetic therapy against such anemia is indicated; it is impossible to expect prompt and effective repair and rehabilitation of tissues to occur without adequate blood supply.

That renal injury occurs is not surprising. It is within the cells of the renal parenchyma that the greatest concentration of intoxicating substances occurs. The kidney's function of ridding the body of noxious substances makes the parenchyma particularly vulnerable.

An acidosis of mild degree is said to occur in the majority of pregnant women. This is usually compensated by the buffer substances. In eclamptic patients the ammonia nitrogen of the blood is increased[45] in further effort at compensation. Acidosis is most pronounced in the intoxicated patients.[46, 47, 48] An increased production of lactic acid occurs in eclampsia.[12, 49] An uncompensated acidosis increases the renal permeability[50] and it has been shown that acid substance causes diuresis.[51] Acidification of the urine causes alkalinization of the cells of the renal parenchyma, and vice versa alkalinization of the urine causes the cells to become acid.[52] In this connection it was noted that in many of these patients the albuminuria increased greatly in intensity upon alkalinization of the urine, only to diminish rapidly with the reappearance of an acid urine. Such variations were noted both in patients on therapy with alkalies or acids and in those receiving no medication whatever. From previous researches[51, 52] and from the clinical observations made on the present group of patients, it may be concluded that alkali administration to the point of alkalinization of the urine in nephritic patients is inadvisable and not without definite risk. Diuresis is best induced with water and, if necessary, acid salts, such as calcium chloride, calcium nitrate or ammonium chloride. Indiscriminate administration of alkalies is to be deplored.[53, 54]

If edema is actually a protective mechanism in intoxicated tissues, deprivation of water is illogical therapy. Nephritis in childhood is far more successfully treated on liberal water allowance, and it has been reported[54] that dehydrating measures may precipitate symptoms of uremia.[59] With complicating cardiac exhaustion the attitude must be one of conservatism as liberal administration of fluids may and does cause acute cardiac dilatation and failure.[26] Attention to the circulatory efficiency, adequate digitalization and correction of anemia will do much toward improving the water balance of edematous patients. During the subsidence of edema the renal concentration test procedure is of course valueless; diuresis with a urine of low specific gravity occurs even though no fluids are taken orally. Edema is essentially a tissue phenomenon and not necessarily renal in origin.[55]

The degree of arterial hypertension is, in many respects, the most accurate clinical criterion of the severity of intoxication.[67] The relative hypertension, however, is more significant than the absolute degree of hypertension in evaluating the intoxication. In the patients of Group C, with preexisting vascular disease prior to pregnancy, the average arterial tension was very high; the relative rise from ante pregnancy levels is not much greater than in the other groups. In a patient nineteen years old, whose arterial tension had been 110/60 early in pregnancy, a blood pressure of 150/100 during the eighth month may indicate an intoxication from pregnancy per se as severe as that occurring in a woman of thirty-four, with an arterial tension of 190/125, if prior to pregnancy a vascular disease with hypertension existed. However, the menace does not lie solely in the intoxication; excessive arterial hypertension itself constitutes a grave menace.[15] Gradual reduction of excessive arterial hypertonia is therefore indicated. This may be accomplished most adequately, gradually, and physiologically by the oral administration of bismuth subnitrate[56, 57] in doses of gr. x, thrice daily. In the presence of profound intoxication as occurs in the preeclamptic form of intoxication, this is useless, or when extensive arteriosclerosis already exists.[58] It has proved most useful in the first group of cases, the nephroses of pregnancy or the syndrome of renal fatigue.[56, 57] It must be remembered, however, that under such therapy the arterial tension becomes a less accurate index to the intensity of the intoxication, and a false sense of security must be guarded against.

Premature termination of pregnancy is justified in certain instances of nephritis in pregnancy as with other complications.[60] In determining the most opportune time for termination of gestation clinical judgment is strained to its greatest responsibility.[66] Judgment must be based upon careful evaluation of the individual problem, weighing and considering both the medical and surgical aspects. Not only is the immediate prognosis a significant criterion but also the effect of con-

tinuing pregnancy upon the future prognosis. Preexistent renal and/or vascular disease is permanently exacerbated and degenerative processes accelerated by pregnancy. Eclampsia is probably most safely and efficiently treated by prophylactic termination of pregnancy in the preeclamptic phase, prior to the onset of convulsions.[15, 67] The syndrome of renal fatigue rarely requires surgical or obstetric intervention.

The prognosis of nephritis in pregnancy varies with the type of renal disturbance as has been pointed out above. A severe intoxication is almost certain to leave a residuum of some irreparable permanent injury and depletion of reserve. The outlook for a subsequent normal pregnancy following eclampsia is less favorable than is generally believed.[61] Chronic nephritis exacerbated by pregnancy offers a poor future prognosis.[14-62] The fetal mortality is high, particularly in the nephropathies appearing relatively early in pregnancy.[63] The late prognosis has been inadequately studied.[64] It may be concluded that the most essential criteria of the immediate prognosis is the severity of the relative arterial hypertension as an index to the severity of the intoxication and the extent of depletion of the renal reserve as measured by the renal concentration test. Evaluation of the future prognosis should be based upon: (1) the degree of anemia; (2) the degree of renal functional impairment; (3) the age of the patient; (4) the promptness with which improvement occurs following obstetric delivery and the degree of such improvement. Of these factors the last is perhaps the most significant. Clinical experience has taught that the earlier in pregnancy evidences of renal injury appear, the more extensive is the renal depletion and the less is the reserve.[66]

SUMMARY

1. Nephritis in pregnancy is clearly divisible into three major classes:
   A. The nephritis of pregnancy (syndrome of renal fatigue in pregnancy).
   B. Eclamptic intoxication.
   C. Preexisting renal and/or vascular disease exacerbated by pregnancy.
2. A fourth group includes all those cases having other complications, such as cardiac disease, thyrotoxicosis, infections, and obstetric difficulties.
3. Each of these groups is clearly defined and retains individual characteristics.
4. The clinical syndrome, date and type of onset, associated changes, mode of therapeutic attack, and the prognosis differ in each group.
5. These differences have been pointed out and discussed.

6. Efficient therapy can be obtained only through proper recognition of the type of renal disease, careful consideration of the causative factors of the renal injury, and constant cognizance of the condition of the patient. It is not the disease which requires treatment, but the patient.

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A STATISTICAL STUDY OF PLACENTA PREVIA AT THE JOHNS HOPKINS HOSPITAL

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FROM the opening of the Department of Obstetrics of the Johns Hopkins Hospital on August 17, 1896, to May 1, 1930, 146 women have been admitted suffering from placenta previa during the last trimester of pregnancy. The number of cases is too small for definitive statistical study, but it represents the experience of thirty-four years in a clinic which has had over 36,000 admissions. For this reason, it has seemed worth while to analyze our material in an effort to appraise the results, fetal and maternal, from the point of view of the type of therapy which may offer the best results in this serious complication of pregnancy; although it must be admitted that whatever conclusions may be drawn are based upon too few cases to be binding. The present time seems peculiarly fitting for such an analysis since a great deal has been written recently concerning the treatment of placenta previa by cesarean section, and since the general policy of this Clinic has been along more conservative lines.

We have studied the material from three angles: first, to ascertain the incidence of placenta previa, both in clinic practice and in the childbearing population at large, with particular reference to the effect of color and parity; second, to learn the results to the mother; and third, to ascertain the outcome to the child.

INCIDENCE

This service has always been practically equally divided as to black and white patients. Likewise, the number of primiparae and multiparae is approximately the same. During the period of almost thirty-five years covered by this report, there have been filed in the Record Room the histories of 36,198 obstetric patients. Of these 22,646 were admitted to the hospital, and 13,552 were taken care of in their homes. As it is the policy to admit at once to the hospital any patient on the Out-Patient Service who develops an abnormality, it seems proper to include such patients in determining the incidence of placenta previa.

In the total admissions to the service the incidence of placenta previa is 1 to 248. If, however, we restrict our study to patients who have been delivered by us after the pregnancy has reached the period of viability for the child, the total cases become reduced to 31,198, and the gross incidence of placenta previa is increased to 1 in 214.

The great majority of the women were registered in the Dispensary for prenatal care, and represent a fair normal cross-section of the

population. On the other hand, 5 per cent of the Out-Patient Service and 11 per cent of the Hospital patients were accepted as emergency cases, and represent a distinctly abnormal population with a very high incidence of obstetric complications. Fifty-seven of the cases of placenta previa fall in the former and 87 in the latter group, while in 2 instances this point was not noted. In other words, the incidence of placenta previa was 1 to 30 in the emergency, as compared with 1 to 499 in the registered patients.

A consideration of the cases delivered in the hospital in the last third of pregnancy brings to light an interesting point, and that is that the incidence of placenta previa is definitely higher in white than in black women, our incidence being 1 in 98, and 1 in 158, respectively. This difference is particularly marked in the white multiparae, as our figures are practically identical for primiparae of both races, 1 to 507, and 1 to 544, respectively; whereas, placenta previa occurred once in every 52 white multiparae as compared with once in every 80 black multiparae admitted to the hospital. No explanation for this significant racial difference presents itself at this time. Indeed, it is contrary to what one would expect from a priori reasoning.

MATERNAL MORTALITY

In the total series of 146 cases there were 16 maternal deaths, an uncorrected mortality of 10.96 per cent. Analysis shows 9 deaths in

TABLE I

TYPE	CASES	MATERNAL DEATHS	MORTALITY PER CENT
	1896-1930		
Central	28	6	21.43
Partial	61	9	14.75
Marginal	57	1	1.75
Total	146	16	10.96
	1896-1909		
Central	7	2	28.57
Partial	9	3	33.33
Marginal	10	0	00.00
Total	26	5	19.23
	1910-1919		
Central	6	1	16.67
Partial	18	2	11.11
Marginal	15	1	6.67
Total	39	4	10.26
	1920-May 1, 1930		
Central	15	3	20.00
Partial	34	4	11.76
Marginal	32	0	00.00
Total	81	7	8.64

93 cases in white women (9.68 per cent), and 7 deaths in 53 black women (13.21 per cent).

In an effort to ascertain whether or not any improvement has occurred in the maternal mortality rate during recent years, and more particularly since transfusion has become a relatively simple procedure, the patients were divided according as they had occurred prior to 1910, between 1910 and 1919, or from 1920 onward; and the results are given in Table I.

It will be seen that the mortality during the past ten years is less than half that during the first fourteen years of the service. This is probably due to the fact that many of the women in the earlier group were delivered by accouchement forcé, that is, manual dilatation of the cervix soon after admission followed by version and extraction; whereas the custom since then has been the employment of the Voorhees bag, with delivery only after the cervix has become fully effaced.

In general, it may be said that the mortality in marginal placenta previa is very low, 1 in 57 cases, whereas partial and central placenta previa offer a much more serious prognosis. Table I shows that the greatest improvement has occurred in the partial type, and that the mortality from the central type is still very high. At the same time, it should be mentioned that many of the deaths occurred in women admitted to the service after severe and prolonged bleeding at home and that several were practically moribund when first seen.

Condition on Admission.—The patients were next grouped according to their physical condition on admission. If the hemorrhage had been slight, the pulse slow and of good tension, and the general physical impression satisfactory, they were classified as excellent. With severe hemorrhage, rapid and thready pulse, air hunger, and a generally unfavorable impression, the condition was considered poor; while when the findings lay between these two extremes the condition was designated as fair.

TABLE II

TYPE	EXCELLENT			FAIR			POOR		
	CASES	MATERNAL DEATHS	MORTALITY PER CENT	CASES	MATERNAL DEATHS	MORTALITY PER CENT	CASES	MATERNAL DEATHS	MORTALITY PER CENT
Central	16	2	12.50	4	1	25.00	8	3	37.50
Partial	48	4	8.33	6	2	33.00	7	3	42.86
Marginal	48	0	00.00	5	0	00.00	4	1	25.00
Totals	112	6	5.36	15	3	20.00	19	7	36.84

Table II shows that the mortality varied from 5.36 to 36.84 per cent according to the condition of the patient when first seen, and that all but one of the deaths occurred in the central and partial types.

Pulse.—The pulse rate on admission was investigated in its bearing upon maternal mortality, since it is one of the best indices as to the condition of the patient.

Table III needs little comment, as it merely shows that the prognosis varies with the general condition of the patient. It is, however, noteworthy that no death occurred among the 33 women whose pulse was below 90 on admission.

TABLE III

PULSE RATE	CASES	MATERNAL DEATHS	MORTALITY PER CENT
Below 90	33	0	0.00
90 to 119	71	6	8.45
120 to 139	28	4	14.29
140 and over	11	4	36.36
Unable to count	3	2	66.67

Extent of Hemorrhage Before Admission.—

TABLE IV

HEMORRHAGE	CASES	MATERNAL DEATHS	MORTALITY PER CENT
None	5	0	0.00
Slight	53	4	7.55
Moderate	37	3	8.11
Profuse	51	9	17.65

Five patients who were admitted to the hospital prior to the onset of labor later developed bleeding and were found to have placenta previa. As with poor general condition and rapid pulse, the highest mortality occurred in women who were admitted after profuse hemorrhage, and was 17.65 per cent.

Cervix.—A few patients were admitted prior to the onset of pains, but in most instances labor had set in before admission and had resulted in varying degrees of cervical dilatation. Table V indicates that in our cases the prognosis became graver as the dilatation increased. In other words, the degree of dilatation affords a rough index of the degree of placental separation and of the extent of hemorrhage. This, however, is not a universal rule, as several patients who were admitted with a cervix less than 3 cm. dilated had bled profusely at home.

TABLE V

CONDITION OF CERVIX	CASES	MATERNAL DEATHS	MORTALITY PER CENT
Closed	17	0	0.00
To 2.9 cm.	47	4	8.51
3.0 to 5.9 cm.	58	5	8.62
6.0 to 8.9 cm.	15	4	26.67
9.0 to fully	5	2	40.00
Unknown	4	1	

Time From Admission to Delivery.—Thirty-four of the patients were delivered immediately after their arrival at the hospital. In many of

these the delivery was effected after manual dilatation of the cervix, in a few by cesarean section, while in the remainder the cervix was sufficiently dilated on admission to permit spontaneous or operative delivery. Eight deaths occurred in this group, or 23.53 per cent. Fifty-two other patients were delivered in less than six hours with 4 deaths (7.69 per cent), 34 were delivered in from six to twelve hours with 3 deaths (8.82 per cent). Thirty-five women were in the hospital over twelve hours prior to delivery and none died. One patient died undelivered three and one-half hours after admission. In other words, we have no indication from this analysis that immediate delivery decreases maternal mortality. Indeed, it would seem that postponing delivery until after the initial shock is over and the patient's general condition improves offers the most favorable prognosis.

Duration of Pregnancy.—It has long been known that a large proportion of cases of placenta previa become manifest before the patient has reached term. That such was the case in our series will be seen from Table VI. The division is made by lunar months rather than by calendar months.

TABLE VI

DURATION	CASES	PER CENT OF TOTAL
6 to 6.9 lunar months	10	6.85
7 to 7.9 lunar months	26	17.81
8 to 8.9 lunar months	30	20.55
9 to term	21	14.38
Term	56	38.36
Unknown	3	2.05
	146	100.00

In other words, about three-fifths of the patients in whom the duration of pregnancy could be ascertained with any degree of accuracy were before term. The white women in general carried the pregnancy longer than did the black, and 43.96 per cent of the former and 30.77 per cent of the latter reached full term; while the average duration of pregnancy was 8.75 and 8.36 lunar months in the two races, respectively. If now the maternal mortality is considered in relation to the duration of pregnancy, we find that 66 patients were delivered prior to the last month of pregnancy. Three of these died, a mortality of 4.55 per cent. On the other hand, 77 cases of placenta previa were delivered at term or during the last month of pregnancy with 12 deaths, a mortality of 15.58 per cent, which is over three times as great as in the premature cases.

Possibly the amount of placental separation and hence the hemorrhage is less in the cases terminating prematurely. Certainly the prognosis becomes increasingly grave as the patient approaches term before the onset of severe symptoms.

Weight of Child.—Since the maternal mortality was found to be lower in the cases admitted prior to the last month of pregnancy, it was

thought advisable to compare it with the size of the child at birth. In 10 instances the weight of the child was not noted; but in the 63 cases in which it weighed under 2500 gm. there were 2 maternal deaths, 3.17 per cent, as compared with 11 deaths or 15.07 per cent in 73 cases in which it weighed 2500 gm. or more. These figures coincide closely with the experience noted in the preceding paragraph, when the mortality was considered according to the duration of the pregnancy. We must admit that the maternal mortality rate is highest in those patients whose babies, from the point of view of weight, have the best chance of survival.

Parity.—Multiparity is considered a predisposing factor in the etiology of placenta previa. Since with multiparity goes an increased obstetric age, these factors were next considered in their influence on maternal death. Twenty-two of the cases in this group occurred in the primiparae, or 15.28 per cent, as compared with 13 (9.03 per cent) in women who had had ten or more previous pregnancies. The average parity of the white women was 4.54 and of the black 4.12. It is interesting to note that of the 28 cases of central placenta previa only two occurred in primiparae and both recovered. Furthermore, in the group of 22 primiparae there was only one maternal death, 4.55 per cent; while in multiparae the average mortality was 11.48 per cent, rising to 23.08 per cent in the group of women who had given birth to ten or more children.

Age.—Table VII.

A study of the age of the mother results similarly. The age of two patients was not given in the histories. Ten women were under twenty (6.85 per cent), and 16 were forty or more years of age (10.96 per cent). The average age for the entire group was 30.30 years, being higher in the white than in the black women, 31.46 and 28.30 years respectively. It appears that the maternal mortality increases with the age of the mother, and attains the high figure of 31.26 per cent in those who had reached the age of forty.

TABLE VII

AGE	CASES	DEATHS	MORTALITY PER CENT
To 20 years	10	1	10.00
20 to 29	53	3	5.66
30 to 39	65	7	10.77
40 and over	16	5	31.25
Unknown	2	0	0.00

Presentation.—The incidence of abnormal presentations has long been known to be high in placenta previa. Such was found to be the case in this series, and transverse, breech, and compound presentations comprised 26.03 per cent of the total. That the maternal mortality in the abnormal presentations (5.26 per cent) was lower than in the vertex (12.96 per cent) is undoubtedly due to the fact that they occur mostly

with prematurity, and we have already seen that the death rate is lower in that group.

Treatment.—The mode of delivery may be briefly indicated. Nineteen women were delivered at once by manual dilatation and version. Cesarean section was practiced in 5 instances. Immediate delivery, spontaneous or operative, with the cervix fully dilated or sufficiently dilated for the size of the child occurred ten times. In 99 patients a balloon was inserted and was followed later by spontaneous or operative delivery. Braxton-Hicks's version was employed in 3 instances, and in 10 in which the head was in the pelvis, the bleeding was so slight as to warrant no therapy. In 26 cases the uterus was packed postpartum. Cervical tears were recorded as severe enough to necessitate immediate repair in only 16 cases.

Puerperium.—The puerperium was febrile (temperature 100.4° on two or more days) in 43 of the 84 white women, excluding immediate deaths. This gives a febrile rate of 51.19 per cent in this race as against one of 65.96 per cent in 47 colored patients. The use of the balloon undoubtedly accounts in part for this high figure.

Analysis of Deaths.—Of the 16 women who succumbed, the death was due to infection in only one instance. This patient, admitted in good condition, bled profusely before a bag could be introduced. After delivery she developed a severe infection and died on the fiftieth day postpartum of thrombophlebitis. One patient with a marginal placenta previa and a markedly contracted pelvis, in whom bleeding had been slight, was admitted in extremis after numerous attempts at forceps delivery by her physician. She was delivered by craniotomy but died a few minutes later of shock, hemorrhage playing no rôle in her death. Another patient died of nephritis two days after cesarean section, the indication for the section, and the cause of death being the renal lesion in this case. The remaining thirteen patients died of hemorrhage and all within eight hours of admission. One was admitted almost exsanguinated and still bleeding. A bag was introduced but she died undelivered before transfusion or other intravenous therapy could be instituted. Five of these patients were admitted in poor condition, two in whom the pulse was so thready as to be uncountable, and all died within two hours of delivery. Two others were admitted in fair condition and died within two and one-half hours of delivery, while the remaining five women were in good condition when received but bled so severely after delivery as to die within four hours. Omitting the six patients who came to the hospital in desperate shape, the death from nephritis and the one due to shock, we reach a corrected mortality of 5.80 per cent, for whose death the Clinic was directly responsible.

Fetal Mortality.—In this series, there were only 47 babies discharged alive from the hospital. Most of the rest were stillborn, although there

were a few deaths from prematurity among those born alive. The gross fetal mortality then was 67.81 per cent, and was lower in the white (63.44 per cent) than in the black race (75.47 per cent). Naturally the mortality was highest in the cases of central placenta previa, being 89.29 per cent. In the partial group there were 77.05 per cent dead babies, which fell in the marginal group to 47.37 per cent.

Many of the babies were premature and the average weight of the white infants was 2698 gm., as compared with 2377 gm. in the black race. As will be seen from the following table, the greater the weight of the baby the better its chance for survival.

TABLE VIII

WEIGHT	CASES	FETAL DEATHS	INFANT MORTALITY PER CENT
To 1500 gm.	17	17	100.00
1500 to 1999 gm.	23	21	91.30
2000 to 2499 gm.	23	16	69.57
2500 to 2999 gm.	23	12	52.17
3000 to 3499 gm.	28	14	50.00
3500 to 3999 gm.	16	5	31.25
4000 and over	6	4	66.67
Unknown	10	10	

In just over a quarter of the cases the child was already dead on admission as the fetal heart could not be heard. This occurred most often in the central and least often in the marginal type of placenta previa. If we omit the cases in which the child was dead on admission, we obtain a fetal mortality of 50.53 per cent. Many of these children were premature, and considering only such babies as were known to be alive on admission and which weighed at least 2500 gm., the fetal mortality was 38.71 per cent.

Finally, an investigation was made as to the effect of the lapse of time from admission to the hospital to delivery, when the fetal heart was present on admission and the child weighed 2500 gm. or more.

TABLE IX

DELIVERY	CASES	FETAL DEATHS	INFANT MORTALITY PER CENT
Immediate	11	5	45.45
0 to 2.9 hours	6	3	50.00
3 to 5.9 hours	18	5	27.78
6 to 8.9 hours	11	4	36.36
9 to 11.9 hours	4	2	50.00
12 and over	12	5	38.71

Although each of these groups is too small for definite conclusions, one nevertheless gains the impression that this factor has little if any effect upon the prognosis for the child and the results are no better after immediate delivery from below than when a number of hours elapse before the child is born.

DISCUSSION

In a service of over 36,000 admissions, and extending over a period of almost thirty-five years, placenta previa occurred in 146 instances, or approximately 1 in 250. Emergency admissions to the hospital service comprise only a small part of the total cases but include a larger percentage of the total cases of placenta previa. Thus, in women admitted as emergency cases and delivered on the service the incidence is 1 in 30, whereas among those registered for prenatal care it is 1 in 500. This last figure seems to represent fairly accurately the occurrence of this complication in a typical cross-section of the child-bearing population.

There is a rather surprising racial difference in the incidence of placenta previa. In a service divided about equally between whites and blacks, and between primiparae and multiparae, it is seen that it occurs once in every 98 deliveries in white women, as compared with once in every 158 in black women. In view of the greater average number of pregnancies among the black women, such a finding is difficult to explain.

The gross maternal mortality for the series was 10.96 per cent. It is comparatively higher in the black than in the white race, being 13.21 per cent and 9.68 per cent respectively. During the early days of the Clinic a number of the patients were delivered immediately after entering the hospital by manual dilatation of the cervix and extraction of the child. This practice was soon given up and since then the hydrostatic bag has been commonly employed. At the present time, the treatment of cases admitted with vaginal bleeding during the last third of pregnancy is as follows: A sample of blood is obtained at once, and preparations made for securing compatible blood donors, with the idea of being ready for transfusion as soon as possible. If the patient's condition is not critical this procedure is held in abeyance for the time being. If, however, the woman is suffering from the loss of blood, an intravenous injection of saline or glucose is begun immediately and is followed by transfusion as soon as the necessary preparations can be made. Meanwhile, the patient is taken to the operating room. All necessary preparations are made for the introduction of a bag. A vaginal examination is now done and if the bleeding is found due to placenta previa, the bag is inserted intraovularly at once. The patient is then returned to bed, mild traction exerted by means of a weight attached to the bag and suspended over the edge of the bed. Immediate delivery is effected after extrusion of the bag, the cervix is inspected for tears, and if there is any bleeding following the third stage of labor the uterus is packed prophylactically. Throughout labor and for some hours after delivery, the patient is constantly watched and donors for transfusion are kept on the delivery floor so that this procedure can be carried out without delay if it becomes

necessary. It is strongly felt that the immediate and free use of transfusion aids materially in reducing the mortality incident to placenta previa.

That the maternal death rate from placenta previa has been lowered in recent years in this service is evidenced by the fact that from 1896 to 1910 it was 19.23 per cent, whereas since 1920 it has fallen to 8.64 per cent.

There is a considerably different mortality according to the type of placenta previa. In a series of 57 cases of the marginal type there was only one death (1.75 per cent); 14.75 per cent of the cases of the partial type terminated fatally, while central placenta previa in this group of cases was associated with a mortality of 21.43 per cent.

As has previously been stated a large number of the patients (87) were admitted as unregistered emergency cases and many of them were in desperate condition when first seen. Classifying the patients as excellent, fair, or poor risks according to the clinical picture on admission, we find a low mortality of 5.36 per cent when the initial examination revealed the woman to be in good condition. This figure rises in the group classed as "fair," and when the situation was deemed ominous on admission, the mortality reaches 36.84 per cent. A study of the condition of the patient from the point of view of hemorrhage before and pulse rate on admission checks the above conclusion closely. It is noteworthy that in 33 women admitted with a pulse below 90 there was not a single death.

In some cases the patients were admitted before the onset of labor, but usually, however, having had pains for a varying period of time. In general, the mortality rate rose with the duration of labor prior to admission and the beginning of therapy as indicated by the amount of cervical dilatation. However, in 17 women admitted with the cervix closed there was not a single death. In most of these the preceding hemorrhage had been slight but some had bled severely.

In view of this observation, a further division of the cases according to the hours elapsing between admission and delivery becomes of interest. The highest maternal mortality (25.53 per cent) occurred in the group delivered immediately after admission. However, in this group are included those who were delivered by accouchement forcé, as well as those admitted with a widely dilated cervix who had been bleeding throughout some hours of labor. On the other hand, there were 35 women who were delivered not less than twelve hours after admission and in this group there was not a single death.

In approximately 60 per cent of the patients the symptoms of placenta previa appeared at varying intervals before the pregnancy had reached term. In general the white patients were farther advanced than the black. Considering the maternal mortality from the point of view of duration of pregnancy, we found a rate of only 4.55 per cent

when the pregnancy ended prior to the last lunar month, whereas it was 15.58 per cent in those patients who were at or near term. Why this difference should exist is not clear, but it seems significant that the highest maternal mortality occurs in the group in which from the standpoint of the survival of the child the mortality was lowest. A consideration of the maternal death rate according to the weight of the child likewise shows a higher figure where its weight exceeds 2500 gm.

An investigation of the parity of the patients in the series showed a low mortality rate of 4.55 per cent in the primiparous women as against a much higher one in the multiparous. A considerable number of the women had had ten or more previous pregnancies and in them the mortality was highest, 23.08 per cent. Being more common in multiparae, placenta previa obviously occurs most frequently in women well along in their obstetric career. In view of this, it is interesting that the highest mortality occurs in women whose age is forty or more. In almost every way, it seems evident that the pregnant elderly women makes a very poor risk.

That we have to deal with a high incidence of febrile puerperia is not surprising, for this is to be expected in any series where operative procedures are the rule and particularly where the hydrostatic bag is commonly employed. However, only one death occurred from infection. It is noteworthy that the incidence of puerperal infection is much higher in the blacks than in the whites, a phenomenon which holds true as well for normal deliveries in the two races.

Analysis of the 16 fatal cases shows hemorrhage to be the most important factor in 13 instances. One woman died of infection, one of nephritis, and one of surgical shock, the result of operative procedures before admission. In 6 of the 13 deaths due to bleeding, the condition of the patient on admission was desperate and if these deaths, the death due to shock and to chronic nephritis, are omitted as not being directly the responsibility of the Clinic, the corrected mortality falls to 5.80 per cent.

The prognosis for the child in placenta previa is always grave, and in this series the gross fetal mortality was 67.81 per cent. This is due partially to the large number of prematurely born infants, and in our series 46.32 per cent, or almost half, weighed less than 2500 gm. The weight of the average white baby was 300 gm. more than that of the black, which coincides with a higher fetal mortality in the latter race. The mortality is highest in the central type of placenta previa and lowest in the marginal variety.

In over a quarter of the total cases the fetal heart tones were absent on the admission of the patient to the hospital. If we omit these cases from discussion (and obviously no form of therapy could alter the results here), and consider only those babies weighing 2500 gm. or

over, where the fetal heart was present on admission, the mortality falls to 38.71 per cent. Thus, it would appear that of the babies, presumably fair risks on admission, over one-third died prior to the delivery of the patient. However, the number of hours from admission to delivery made no difference in the fetal mortality and, indeed, is lower in the group delivered twelve or more hours after entering the hospital than when immediate evacuation of the uterus was practiced.

After the above considerations, what can be said concerning the treatment of placenta previa? The value of prompt and if necessary repeated transfusions seems to be without question. Very probably immediate delivery by cesarean section after admission of the cases at or near term and where the fetal heart was still in good order would result in more live babies. What effect such a procedure would have upon the maternal mortality is entirely problematical. Certainly the bag gives entirely satisfactory results in the marginal type of case. Many of the other cases are admitted in too poor condition to risk a laparotomy. In still others, bleeding is so profuse that it must be checked at once, or before any abdominal operation can be performed. Many have already had unsterile examinations on the outside before admission, some of them entering the hospital with the cervix packed, and in them indiscriminate use of cesarean section would probably increase the mortality from sepsis. It is the feeling of this Clinic at present that this operation has only a restricted scope in the treatment of placenta previa. In a central placenta previa with the cervix closed or just opening and with a viable child whose heart tones are in good order it seems permissible. In a multipara in good condition, with several live children, where sterilization seemed a reasonable procedure cesarean section with hysterectomy or tubal excision might not be condemned. In an occasional case the desire for a live child might counterbalance an increased chance for mishap to the mother. Except in these instances the use of the bag still holds as the procedure of choice, though far from an entirely satisfactory one.

CONCLUSIONS

1. The incidence of placenta previa in an average childbearing population is about 1 in every 500 deliveries. It is higher in white than in black women.

2. The maternal mortality in placenta previa is still high (8.64 per cent), although the results have improved greatly in the past thirty-five years. It could be still further reduced by the prompt hospitalization of all bleeding cases and more frequent employment of transfusion.

3. When the patient is admitted in good condition, with low pulse and before the hemorrhage has become alarming, the mortality is low and does not rise if a number of hours elapse before the patient is

ultimately delivered. The mortality is highest in those patients who are delivered immediately after admission, or before the general condition has been improved by intravenous therapy.

4. The incidence of premature labor is high, but the maternal mortality in this group is low and increases more than three times when delivery occurs at or near term.

5. About 15 per cent of the cases occur in primiparae. The incidence of central placenta previa in this group is low (9.10 per cent). The maternal mortality is much higher in multiparae and also increased as the age of the patient rises.

6. Puerperal infection occurred in over half of the cases in this group. However, only one death from infection is recorded.

7. Hemorrhage accounts for 13 of the 16 deaths in the series. Several of the women were admitted almost moribund, and omitting these as well as deaths from causes unrelated to placenta previa, the mortality falls to 5.80 per cent.

8. The prognosis for the child is grave. About one-half of the children weigh less than 2500 gm. at birth. In more than 25 per cent of the cases the fetal heart was absent on admission. Omitting these two groups, the stillborn and neonatal mortality is still very high, 38.71 per cent.

9. The treatment of placenta previa is still unsatisfactory; liberal transfusion offers the best method of reducing the mortality. The hydrostatic bag offers satisfactory results in the marginal type of case. The indiscriminate use of cesarean section, while increasing the chances for the child, would probably not reduce the maternal mortality. Many of the patients who succumb are too ill on admission, or bleeding too severely to warrant laparotomy. Others, due to unsterile examinations on the outside or the use of vaginal packs, are admitted potentially or obviously infected and in them the use of cesarean section, unless followed by hysterectomy, would be fraught with considerable danger. Cesarean section may, however, be indicated in cases of central placenta previa admitted in good condition before or early in labor, and with a living and viable child; or where the desire for a live child counterbalances any increased risk to the mother.

THE RADIATION TREATMENT OF AMENORRHEA AND STERILITY. WITH A REPORT OF CASES SO TREATED

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IN NO other subject of medicine is there so much confusion and misunderstanding prevalent as in the application of radiant energy in gynecology. Indeed the situation is such that both layman and physician regard the employment of x-rays and radium only as destructive elements. When unlooked-for disagreeable sequelae follow therapeutic uses of radium and x-rays, the whole procedure is condemned and other patients are hindered from seeking its benefits. However, in no field of treatment of the female sexual phenomena is it more helpful and more promising of spectacular results than in that of functional disorders of the ovary. In cases of sterility, where it is desired to produce offspring, radiation plays the rôle of a guardian angel in fostering a happy married life which would otherwise be barren and dreary.

Recently, however, and very regrettably, doubts appear to have been cast on the safety of this form of therapy. In the daily press not long ago there appeared an article by an alleged expert to the effect that abnormal babies or monstrosities were born of irradiated mothers. Another item, receiving equally important publicity, claimed the control of the sex of the unborn child through irradiation. Then, too, there are some honest, industrious, ethical medical men who seek out the oddities of therapeutic methods, quote statistics of rare occurrences of abnormalities, as if the latter all occurred in one associated sequence, and from such jumbling of unrelated facts draw conclusions as to supposed evils of radiation therapy.

The early workers with the x-rays and radium, noted the biologic reaction of tissues to these rays without at first clearly understanding them. The results usually were destructive. As more careful study led to better understanding of the principles of radio-activity, it was noted that radiant energy either stimulated the tissues, destroyed them, or did not affect them at all. Early in this study Bergonie and Tribondeau were able to conclude that the more embryonic the tissue the more it responded to radiant energy, and the more defined, adult, or highly differentiated the cell, the more resistant it was to radiation. The effect on gonads has been studied by Regaud, Lacassagne, Schinz, Dobrovalkaia and others. The male cells are easily affected but recuperate readily and, according to Dobrovalkaia, such male cells as are damaged by radiation and recover do not, if subsequently used in

impregnating the female, transmit such malformations. As yet no one has ever followed an injured male cell and there is no positive proof that the offspring is adversely affected by such injured cell. In Ewing's opinion, normal tissue is ordinarily unaffected by the proper therapeutic use of radiation.

The biologic action on the ovary is still undetermined. The true pathologic picture of the ovary of a woman menstruating irregularly or not at all, or in women incapable of becoming pregnant, is still unknown. The problem of sterility, which was known in Biblical times, is difficult of explanation in every case, due to the complexity of the factors involved in the phenomena causing pregnancy. Rubin, in his discussion of this subject advises consideration of all extraneous factors before attempting therapeutic interference with the ovaries. As he sees it, the aim and effect of therapy in female sterility is to correct abnormalities and to restore anatomic relations and, if possible, functional conditions to as nearly normal as possible. For the correction of the functional conditions he has recommended the employment of fractional doses of x-rays, and it was at his suggestion that I began this work in 1924. Rubin reports that over 50 per cent of his patients so treated satisfactorily became pregnant. At The Mayo Clinic, Drs. Dripp and Ford have found that irradiation is particularly applicable in cases of menstrual irregularity, whereby, excluding all other etiologic factors, an inherent disturbance of the ovaries may be assumed. Whether or not menstruation is wholly controlled by the ovary or is the result of a combined action of secretory glands distributed throughout the body, is still not thoroughly understood. In his definition of the menstrual phenomena, Howell states that the phenomenon of menstruation is dependent on the periodic activity of the ovaries, and that in most cases menstruation is connected with ovulation, the ripening and discharging of a graafian follicle.

Anspach says that ovarian impulse and uterine response are essential to the menstrual flow. The corpus luteum forms a stimulus for the next menstrual period, follicle-bearing tissue must be present in the ovary to cause menstruation, and menstruation is a complicated process of which the most obvious evidence is the menstrual flow. He says, too, that the ovary has an internal secretion which gives rise to menstrual molimina.

Westerman, however, says that in mice ovarian function proceeds normally even if the uterus is extirpated.

In his study of the circulation of the ovary, Clark states that the increased amount of blood sent to the pelvic organs during the menstrual period causes a marked augmentation of the intracapsular pressure of the ovary which results in the bursting of the graafian follicle, after which expulsion of the ovum takes place. Ovulation occurs from fourteen to sixteen days after the beginning of menstruation and then the corpus luteum begins to grow. Ovulation causes menstruation; copulation assists the ovulation, and expulsion of the ovum occurs when the graafian follicle bursts.

Reynolds says that the ovaries of sterile women on gross examination show numerous thin-walled projection follicles or numerous small imperfect corpora.

Frank believes that there is a secetory controlling hormone supplied by all the sexual glands of the body. Frankel thinks that this hormone is made up of the yellow body cells of the corpus luteum. From the standpoint of irradiation I have seen alteration of ovarian function result from the radiation of glands other than the ovaries.

Eden and Lockyer state that for menstruation there must be fully developed activating ovarian tissue and that there is some physiologic coordinating connection between the ovary and other endocrine glands. In their opinion, the chief exciting

cause of menstruation is an internal secretion of the ovary, for ovulation can occur without menstruation and vice versa. There is an ovarian hormone which excites menstrual change in the endometrium, and there is a connection between the thyroid and the ovaries.

These are all suppositions not based on positive experimental data.

Miss van Herwerden from her researches says that in monkeys there are two periods: one, when menstruation occurs with a corpus luteum and the other, when menstruation ensues without the occurrence of ovulation. Therefore, she concludes that the cause of menstruation is somewhere outside of the ovary.

Nemenow reports that in the x-ray treatment for pituitary tumor a concomitant amenorrhea was cured. Dripp has shown that small doses of x-rays to the thyroid, spleen, and pituitary areas have cured functional disorders of the ovaries.

For the control of excessive bleeding in virgins, Seitz and Wintz early made use of irradiation of the spleen with good results. Hofbauer, in 1922, before the German Gynecological Congress, suggested x-ray therapy of the pituitary for gynecologic functional disturbances, especially the effect on uterine myoma after such irradiation. Werner found that x-rays applied to the hypophysis stimulated menstrual reaction, and Borok suggested pituitary radiation for mitigating the climacteric symptoms of early menopause. Frequently, radiation stimulation of the thyroid has effected normal menstruation.

Neither the action of radiation on the ovary nor the latter's reaction to radiation is as yet clearly explained, and the mechanism of ovulation is still unknown. Histologic examination of the ovary shows the ovum lying in a mature graafian follicle surrounded by the cells of the germinal epithelia. In maturing there is a thinning of the follicular wall with increased liquor folliculi which consequently, therefore, increases intrafollicular pressure and results in the rupture of the graafian follicle and discharge of its ovum. The follicle then is filled with blood from the tearing of the vessels in the theca or covering layer, which later develops into the corpus luteum. Hartman believes that usually the corpus luteum must be present for menstruation to occur, but he has found that in the monkey, mere rupture of the graafian follicle brought on menstrual phenomena. It is, I believe, the presence of this corpus luteum that inhibits menstruation during pregnancy. Snyder, however, does not believe that the activity of the corpus luteum inhibits ovulation in primates, while Hartman, from his studies on the opossum, believes that the destruction of the corpus luteum induces destruction of the fetus and he therefore concludes its presence is necessary for pregnancy. But he believes the corpus luteum is not the cause of menstruation in the monkey. Nor is it necessary for the menstrual cycle, nor does the follicular apparatus of the ovary cause menstruation. Kast says the corpus luteum of pregnancy is of increased size and gives off internal secretions.

Experiments by Corner and Allen have shown that removal of the corpus luteum during pregnancy causes the termination of the pregnancy, and these workers therefore conclude that the presence of a corpus luteum is necessary for the pregnancy to continue.

Whitehouse says that the decidua of the upper segment of the uterus is the favorite place for the implantation of the zygote and that this decidua depends for its existence on the integrity and normal function of the corpus luteum.

Johnstone says that the reproductive cycle begins in the ovary just prior to ovulation with the maturation of the follicle, and the formation in the entire ovary, not merely in the follicle or ovarian stroma, of an ovarian hormone. As soon as ovulation has occurred, luteum tissue is formed; this creates a second hormone, which governs and stimulates the preparation in the uterus for the fertilized ovum.

We know that the x-rays have in themselves a power to stimulate. Flattau, Seitz, and Wintz declare that there is a definite stimulation effect by x-rays on the ovaries. Aschoff, Colwell, and Russ have shown that x-rays act directly on the follicular elements of the ovary, while Robinson says that only the tertiary follicles are sensitive to radiation, leaving the primary follicles to continue to ovulate after the x-ray effect has passed. Hirsch believes the action is directly on the corpus luteum; the graafian follicle is embryonic tissue and this is highly sensitive to x-rays. Lenke believes a pathologic graafian follicle, preventing the ripening of a normal follicle capable of producing menstruation, is destroyed by the x-rays, and then leaves the primary follicle free to develop. If we deem this tissue to be so radiosensitive, we can regard the action of irradiation on the ovary at this time as an action directly on a most radiosensitive tissue, which responds by releasing its inhibitory reaction on the ovary, thus allowing the usual menstrual cycle to occur.

Johnstone says that operation on a woman in the latter half of her menstrual cycle with removal of the maturing corpus luteum will cause menstruation to follow in thirty-six hours.

Hartman says the follicle in the corpus luteum is unnecessary for menstruation but the ovary is necessary; therefore, we must look to some endocrine cause within the ovary, perhaps in cooperation with other glands, for example the pituitary, and perhaps the x-rays stimulate such active hormone, causing menstruation. The anterior lobe of the pituitary, according to Johnstone, gives off two types of activating factors: the first one activates the whole ovary, leading to ovulation and the formation of lutein tissue, and a second activator which affects the corpus luteum produced by the first activator; and, he states further that these pituitary factors work only through the medium of an ovary.

Novak claims that the ovum is not the cause of menstruation, because in monkeys definite periodic bleeding occurs without ovulation; that in as much as the follicle and corpus luteum are not the cause of menstruation, the corpus luteum is important only in the preparation of the premenstrual hypertrophy of the endometrium. Novak believes also that the pituitary gland has a periodicity in function and this regulates menstruation.

Johnstone, however, suggests that the activity of the anterior lobe of the pituitary body is maintained by stimuli of a hormone formed by the trophoblasts of the ovum and that existence of this trophoblast in the uterus depends on the function of the corpus luteum.

Zondek and Aschheim, in their experiments looking toward replacing the function of the ovary with other endocrine gland elements in the body, proved that the pituitary gland produces its effect only when the ovary is present and does not work in ovariectomized animals. They call it the motor of the ovary, for the pituitary transplanted on an ovary acted as a motor of the ovary, speeding up its activity. Smith and Engle have shown, from their experiments with the pituitary body, that ovulation is enormously accelerated. Corner denies that there is a specific sex hormone, as Frank declares, but believes that there is a distinct specific corpus luteum hormone.

When we consider that following the radiation of glands other than the ovaries menstruation takes place, we must think of radiation as a direct stimulating agent. We do know that the first reaction to irradiation is a hyperemia, with increased vascular effect in the local area treated. It remains to be proved, however, that this mechanical hyperemia does in some way burst the unripened graafian follicle and thereby set in motion the menstrual machinery. That direct radiation

on the ovary does cause a reaction in the theca with subsequent rupture of a graafian follicle and menstruation, we have seen experimentally, but the biologic reaction and the exact mechanism of it are still unexplained.

Evidently the cure of amenorrhea, as Johnstone suggests, has to do with the uterus, the ovary, and the pituitary. Sterility may often be due to a persistent corpus luteum or in the human being it may be due to the excessive action of the Type II pituitary hormone.

Naujoks believes that the resumption of ovarian activity following temporary cessation after x-ray treatment, is due to the ripening of the undamaged primordial follicles rather than to a restoration of slightly damaged follicles or a renewal of activity of the germinal epithelium. He says that the adult ripened follicle which controls the next menstruation is usually destroyed by x-rays, but the ovum may not be, and it then proceeds to ovulation with only partial x-ray destruction. It may be fertilized, but usually does not proceed to develop, and finally aborts. The later ripening follicles are less radiosensitive and, though slightly damaged at first, recuperate to go on to perfect fertilization and development.

As regards the effects of irradiation on the mother and on the oncoming progeny, there is much confusion and many conflicting explanations. Aside from creating a mild dysfunction, most workers agree that but little untoward reaction takes place in the mother. It is concerning the effect, however, on the unborn child or subsequent effect on future impregnations, and the effect on the future development of the child born following ovarian irradiation of the mother, that various conflicting hypotheses have been offered. It is true that irregularly formed, abnormally formed, and subsequently maldeveloped offspring have been seen following irradiation of the mother.

Döderlein states that the reports of deformities of progeny of radiated mothers have not been proved, and reports of 42 pregnancies constitute his proof that irradiated mothers can give birth to normal offspring years afterward.

Werner, too, reports on 24 such pregnancies, but says that the usual irradiation of the mother does not necessarily cause permanent amenorrhea, even when they are treated with large doses. This has also been shown by Beclere, Stern, myself and others. Such women may subsequently become pregnant, as reported by Schmitt, Nurenberg, Döderlein, Williamson, and myself.

Schmitt reports in detail the results of 22 cases of irradiated mothers for various conditions who subsequently have 39 pregnancies with no abnormal births. In the 8 women treated with stimulation x-rays, there were 17 pregnancies with 12 living normal children.

That workers with radiation elements may marry and produce normal children has been shown by Naujoks who reviewed the cases of 91 mothers having 129 children. Of these only 9 were abnormal, and for 4 of these children other than radiation reasons were found for the abnormalities. This leaves a percentage of abnormalities not exceeding that occurring in progeny of women never irradiated.

It is unfortunate that the fact that irradiated mice have produced abnormal progeny has been utilized as a basis for prohibiting radiation on human beings. Although Bagg in his work with mice has produced abnormal forms, Levine, working along the same lines, failed to substantiate Bagg's findings. Moreover, Krupski and Eisenberg, experimenting on white mice, showed that irradiation did not cause abnormalities unto the third generation. Martius, while granting that abnormal results do occur in animal experimentation, does not feel that we can apply these conclusions to human beings. Robinson, too, claims that irradiation of animal ovaries is not the same as irradiation of human ovaries and that ovarian irradiation is free from harm to offspring.

Whitehouse says that every form of abnormal ova and monstrosity can be produced from normal ovaries and spermatozoa by artificial interference with the environment.

From a statistical study of the literature, Murphy classifies the abnormalities in children of irradiated mothers and concludes that pregnancies in such cases should be interrupted in order to avoid the possibility of producing monstrosities. It must not be forgotten, however, that monstrosities have occurred in women who have never been radiated. Flaskamp states that practical experience and not conjectures should govern the question of whether or not to irradiate human ovaries. He notes that there is an absence of proper reporting of results in the experimental irradiation of ovaries, no distinction being made between the weak doses leading to temporary and permanent sterility, and he does not believe that all reported so-called child injuries are due to the effects of previous irradiation. The births of normal children following x-ray treatments have been reported in a large series of cases by Flatau, Werner, Döderlein, Krups, Rongy, and Rubin. Williamson reports the case of a normal full-term baby born of a mother irradiated while pregnant. Schiller reports the case of a woman, forty-five years of age, in whom a full-term normal pregnancy followed x-ray therapy for myoma, and concludes from this that x-rays in this case stimulated a normal endometrium, making it capable of supporting gestation, which is was not able to do before treatment.

Radiation during pregnancy, however, is a dangerous procedure and may lead to fetal abnormality and destruction.

In our series we had 100 patients and 16 normal healthy children were born of irradiated mothers.

As advised by Rubin, all extraneous factors which might be the causative agents in any specific case were ruled out before x-ray therapy was attempted. In fact, no patient is accepted for radiation who has not been examined and passed upon by a competent gynecologist.

All cases herewith reported have been treated with high voltage x-rays, with the following factors: 200 KV, 4 MA, 0.5 mm. copper and one mm. aluminum filter and had administered on the ovaries a dose of 10-12 per cent. Treatment was given over the right and left anterior and posterior ovarian areas with alternate doses about one week apart. Inasmuch as the endocrine glands are in some way correlated in their action with ovarian functions, patients in whom distinct glandular deficiency was present, were given additional stimulating radiation to the pituitary or thyroid areas and in severe cases to both, with the idea of assisting the ovarian reaction. The successful results of such irradiation, which have been shown by Dripp and Ford, make this method one of choice in glandular dysfunction with ovarian irregularity. In this series this additional irradiation was used successfully in several cases. Especially useful was it in patients to whom a primary ovarian stimulation series had been given, resulting in subsequent pregnancy but which pregnancy terminated in an abortion and recurrent amenorrhea. Direct irradiation in such a case resulted in restoration of menstruation. In patients in whom ovarian radiation resulted negatively, treatment of the pituitary or thyroid brought on menstruation.

There were 100 cases treated, 15 single, 85 married. The symptoms were:

Amenorrhea	82
Associated sterility	62
Irregular menstruation	3
Irregular menstruation with sterility	10

The amenorrhea in these patients varied from eleven months to three years.

The ages of those treated were:

Single, youngest seventeen years, oldest thirty-two years.
Married, youngest nineteen years, oldest forty-five years.
Most of these patients were in the age group of 24-28 and 30-33 years.

Results:

Single:	Treated	15	No result	6
	Menstruated	7	Unknown	2
Married:	Treated	85		
	Menstruated	55		
	Pregnancies	22		
	No result	25		
	Unknown	5		
Babies born:				
	Twins	1		
	Boys	5		
	Girls	9		

Had two or three pregnancies after treatment	4
Pregnant and aborted	3
Still pregnant	3

CONCLUSIONS

The biologic action of the ovary and its intimate connection with menstruation and the question of the control of associated endocrine glands, especially of the pituitary, is not as yet clearly understood.

For the correction of female functional disorders the x-rays have proved efficacious, either when applied to the ovary or pituitary gland or other glandular areas.

The reaction to radiation is not as yet clearly understood. Normal children have been born of irradiated mothers and when properly given, x-rays are neither harmful to the mother nor to the offspring from such irradiated mothers.

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THE ARSENIC CONTENT OF THE HUMAN PLACENTA FOLLOWING ARSPHENAMINE THERAPY

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IT IS generally recognized that the treatment of syphilis in the pregnant woman is singularly beneficial to the fetus. Thus, it is a common observation that patients with a four plus Wassermann reaction and other obvious stigmata of syphilis, give birth to nonsyphilitic infants following a course of therapy which would ordinarily be regarded as inadequate to affect the progress of the disease in adults. Moreover, it is the usual experience that such infants remain clinically and serologically free from congenital syphilis. While it seems probable that pregnancy itself exerts an ameliorating effect upon the signs and symptoms of maternal syphilis[1], it appears equally evident that this beneficial action is not always extended to the fetus, which frequently succumbs to the disease in utero unless the mother has been treated.

This striking contrast between the fate of the fetus in treated and in untreated mothers suggests that antenatal therapy may exert some specific action upon fetal tissues. Although the exact mechanism responsible for such an effect is not known, it has been suggested that the placenta may exert some protective function, that it may possess some vitalistic property of keeping the drug in greater concentration in the fetal circulation, and that on account of the marked vascularity of that organ, a greater and more direct action of the drug is exerted upon the spirochetes in the fetus and in the placenta. Unknown immunologic reactions on the part of the fetus have also been cited as possible explanations. In 1923 Underhill and Amatruda[2] injected pregnant rabbits intravenously with large doses of neo-arsphenamine and showed that twenty-four hours later a substantial quantity of arsenic was still present in the placenta, an amount almost equal to that stored in the maternal liver. These authors believe that their experiments offer a definite answer to the question under discussion, since their results show a storage of arsenic in the placental tissues. As is well known, however, conclusions drawn from experiments on the placentas of lower animals are not necessarily applicable to the human placenta, which differs decidedly in structure from that of the rabbit. Moreover, it may be noted that the amounts of drug administered by Underhill and Amatruda were five times the usual therapeutic dose for human beings.

The present study comprises arsenic determinations on 21 human placentas from patients who had been receiving prenatal arsphenamine therapy. After some 10 placentas had been analyzed, it was thought that the results would be more significant if the placentas were divided into fetal and maternal portions, and each portion analyzed for arsenic; in the last 11 placentas studied this procedure has been carried out by a technic to be described shortly.

METHODS

After the placenta had been washed to remove gross blood, arsenic determinations were made on 20 gram portions by the method of Gutzeit as described by Scott.[3] Control determinations on placentas of patients who had not received arsphenamine were made at frequent intervals and were always found negative. Furthermore, arsenic-free placental tissue, to which had been added known amounts of arsenous oxide, was used for standardization. In the 20 gram portions of placenta taken for this purpose, differences of 5 mmg. in the amounts of arsenous oxide added could easily be detected and it therefore seems probable that the results reported in this paper (mmg. per 100 grams of placenta) are accurate to within 20 mmg. It should be particularly noted that the findings are expressed in micro-milligrams (thousandths of a milligram) of arsenous oxide.

The separation of the maternal from the fetal portion of the placenta was accomplished by laying the washed placenta on a flat surface with the fetal aspect down and shaving the maternal surface with a long, sharp knife, care being taken to secure only a superficial layer of from 2 to 3 millimeters. We are aware that such a method of division represents only an approximation, and that what we designate as the maternal portion likewise contains a certain quantity of fetal elements. We believe, nevertheless, that if the layer removed is sufficiently thin, the bulk of it will consist of maternal tissue only.

RESULTS

The results of the study as shown in Tables I and II indicate that arsenic is retained by placental tissue as long as fifteen days after the last injection of arsphenamine. The amount present during the first three days is relatively large, ranging over 100 mmg. per 100 grams of placenta. Furthermore, it may be noted that a definite cumulative retention of arsenic is manifested, the duration of retention being in part a function of the number of weekly treatments. Thus, Case 1, in Table I, showed no placental arsenic eight days after a single injection, while Case 9, which had received six weekly treatments, showed 40 mmg., although fifteen days had elapsed between the last injection and delivery. Likewise, the findings listed in Table II leave little doubt that the retention of arsenic by the human placenta occurs

chiefly in the fetal portion. It will be observed, indeed, that the quantity of arsenic found in the fetal portion of the placenta is often three and four times greater than that present in the maternal part. When, furthermore, it is recalled that the method used for separating the two parts of the placenta does not preclude the presence of some fetal tissue in what we call the maternal part, it seems likely that the actual maternal tissue really contained even less arsenic than our figures indicate.

TABLE I. SHOWING ARSENIC CONTENT OF PLACENTA AT VARYING INTERVALS AFTER ARSPHENAMINE THERAPY

CASE NO.	NO. WEEKLY TREATMENTS	DAYS BETWEEN LAST TREATMENT AND DELIVERY	DRUG	DOSAGE GRAMS	PLACENTAL ARSENIC MMG. PER 100 GM.
1	11	2	N*	0.6	160
2	5	4	N	0.3	120
3	9	5	A*	0.3	80
4	5	5	N	0.45	90
5	2	5	A	0.4	60
6	15	6	A	0.2	100
7	1	8	A	0.3	0
8	6	15	A	0.3	40
9	6	15	N	0.4	60
10	10	30+	A	0.3	0

*N = Neoarsphenamine, A = Arsphenamine.

TABLE II. SHOWING THE DIFFERENCES BETWEEN THE ARSENIC CONTENTS OF FETAL AND MATERNAL PORTIONS OF PLACENTA AFTER ARSPHENAMINE THERAPY

CASE NO.	NO. WEEKLY TREATMENTS	DAYS BETWEEN LAST TREATMENT AND DELIVERY	DRUG	DOSAGE GRAMS	PLACENTAL ARSENIC MMG. PER 100 GRAMS	
					FETAL	MATERNAL
1	3	1	N*	0.6	150	80
2	1	1	A*	0.3	120	80
3	3	2	N	0.6	180	100
4	8	2	A	0.2	160	40
5	6	3	A	0.3	120	40
6	11	5	N	0.45	80	40
7	5	9	A	0.3	60	Trace
8	4	10	A	0.3	40	Trace
9	6	10	A	0.3	60	20
10	5	14	A	0.2	40	Trace
11	6	32	A	0.3	0	0

*N = Neoarsphenamine, A = Arsphenamine.

Analyses of the umbilical blood for arsenic in three cases of this series were negative, as were also determinations on the livers and kidneys of a stillborn fetus whose mother had recently had a single injection of arsphenamine.

COMMENT

Upon first consideration, the evidence thus far advanced affords a satisfying explanation of the beneficial effects of antenatal arsphenamine therapy upon the fetus. Certainly, the concentration of a truly

spirocheticidal substance in the chorionic tissues, by presenting a barrier to the spirochetes as well as by "feeding" infinitesimal amounts of the drug into the fetal circulation, would provide as complete a protection to the fetus as could be desired. The question at once arises, however, as to whether the arsenic retained by body tissues is therapeutically active—a query that some students of the subject would answer in the negative. Thus, Kolls and Youmans[4] believe that the appearance of arsenic in a particular tissue is not the best evidence that arsphenamine was deposited there, since it is possible that the original molecule may have undergone considerable change elsewhere in the body with the result that simpler products were liberated in the circulation to appear at some distant point. In this connection the experiments of Kolmer[5] seem particularly significant. He employed three sets of rats that had been infected with Trypanosoma equiperdum. Into the first group he injected suitable amounts of a saline emulsion made from the livers of rabbits which had received weekly injections of 0.03 gm. of arsphenamine for six weeks; into the second group no injections were made, while in the third group he treated the rats with arsphenamine containing the same amount of arsenic as the saline emulsion. In the first and second groups no spirocheticidal effect was observed, all of the rats dying in from five to seven days; in the third group, however, all of the animals survived. As Kolmer, himself, points out, experiments of this kind are not conclusive, but they nevertheless suggest that some of the arsenic stored by body tissues is therapeutically inactive.

That a portion of the retained arsenic, on the other hand, does not lose its therapeutic potency is attested by the investigations of Voegtlin and his associates. In an extensive series of studies these workers showed that the parasiticidal action of the arsenicals is governed by the rate of excretion of the arsenic from the body, those arsenicals which are slowly excreted possessing a high parasiticidal value and vice versa. In this connection, they further demonstrated that the trypanicidal action of arsphenamine could be greatly increased experimentally by ligating the ureters or bile duct, the usual avenues of excretion of the arsenicals. As a result of their studies, Voegtlin and his coworkers,[6, 7] regard the temporary retention of the drug by the tissues of the host as an essential requirement for the chemotherapeutic action of arsenicals. They conclude that the secret of the practical value of arsphenamine and its substitutes is to be found in the fact that these drugs per se are not toxic and are deposited in the tissues immediately after injection. The deposited drug is then gradually converted by means of oxidation into the pharmacologically active, trivalent "arsenoxide." This latter compound on account of its relatively slow and prolonged formation exerts its toxic effect upon the

parasites during a long period of time. When further oxidation takes place to pentavalent arsenic, this compound is rapidly excreted.

It seems probable then that the retention of arsenic by the fetal portion of the placenta may be an important factor in the successful antenatal treatment of syphilis, although sweeping implications would be hazardous, since a portion of the retained arsenic is probably not therapeutically active.

CONCLUSIONS

1. Following antenatal arsphenamine therapy, arsenic is retained by the human placenta over periods as long as fifteen days after the last treatment.

2. The duration of the retention is conditioned in part by the number of weekly injections the patient has had, a definite cumulative retention of arsenic being manifest.

3. The retention of arsenic by the human placenta occurs chiefly in the fetal portion, which often contains three or four times the quantity demonstrable in the maternal part.

4. The storage of arsenic by the human placenta, and particularly its greater concentration in the fetal part, may be an important factor in the beneficial action upon the fetus resulting from arsphenamine therapy.

It is a pleasure for the writer to thank Dr. Williams not only for suggesting this problem, but for his interest and help throughout the study.

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The author reports a patient, aged thirty-three, with a history of two premature children delivered by forceps with great difficulty, neither one living. Twelve years previously an operation for prolapse had been performed and two and one-half years ago the cervix had been removed and treatment for some type of vaginal infection had been initiated. On her entry to the hospital a well-developed child was palpated abdominally. On vaginal examination no cervix could be made out, the upper portion of the vaginal vault was closed by heavy scar. The author elected to do a cesarean section and remove the uterus. The convalescence was uneventful. The atresic condition was due to a combination of postoperative cicatrization and a subsequent persistent low-grade infection.

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THE COORDINATION OF THE UTERUS IN LABOR*

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THE uterus during pregnancy and labor is generally considered as a whole anatomically and physiologically. In the literature, references are found showing that not infrequently the uterus manifests asymmetrical contractions and tonus states, contraction rings, and other conditions known as, "obliquity of the uterus," "asymmetry of the uterus in early pregnancy," and "placental site paralysis." One of us (Rudolph) has observed the above-named conditions and believes that the mechanism is due to the fact that the uterus anatomically and physiologically is fundamentally a bilateral organ, and in abnormal states may contract arhythmically or asymmetrically. In this paper we will present an argument supporting the theory that the uterus possesses a coordinating mechanism which coordinates the motor activity not only of its sagittal halves but also of its transverse segments or portions.

A review of the literature demonstrates that the uterus in pregnancy and labor may contract irregularly or partially, but no explanation of the mechanism involved is offered. DeLee[1] has observed an irregularity in the time of onset of contraction in different portions of the uterus, the contractions starting in one portion and apparently spreading over the remainder. Cazeaux and Tarnier[2] and Commandeur,[3] have reported that the contractions may be irregular and partial, only an angle of the fundus uteri contracting. Hodge[4] has seen irregular contractions of the fundus uteri, and occasionally at one of its angles. Leischman[5] has observed irregular action, in which the whole organ was not symmetrically contracted, and by palpation, the hand over the abdomen, could detect inequality on the surface of the contracting organ, which was associated with prolonged labor. Smith[6] has seen one lateral half of the uterus to contract while the other half was relaxed. Duncan[7] has written that before inversion of the uterus can occur, there must be irregular action of the fundus uteri associated with paralysis of the whole or part. Bar[8] and Kerr[9] both reported that spasmodic contractions at the orifices of the fallopian tubes caused them to make a diagnosis of ectopic gestation. Cameron and Webster[10] have also referred to spasmodic contractions at the orifices of the fallopian tubes. Duncan[11] has also cited the cases of Lougier and Campbell in which dilatation of one of the orifices of the fallopian tubes was found during labor and at postmortem examination. Jaschke[12] has suggested that "partial inversions" might be caused by traction or by relaxation of circumscribed portions of the uterine wall and contraction of the adjoining portions. Soleri[13] reported a case with a painful circumscribed tetany of the gravid uterus with premature detachment of the normally inserted placenta. Hysterectomy was done, and the uterus showed a tumor of the right horn which gradually disappeared under observation. He expressed the opinion that in a certain number of cases of abortion

*Read at a meeting of the Chicago Gynecological Society, May 29, 1930.

the cause is not a sudden contraction of the whole uterus, but only of a section of its walls, and often of that section on which the placenta is inserted. Holmes[14] stated that paralysis of the placental site of Rokitansky is a distinct physiologic inertia of the placental site, which is approved by Veit, Kiwisch, and Barnes. Barnes[15] has suggested that the orbicular muscles of Ruysch, contracting concentrically, would lessen the area of the uterus and cast off the placenta. Rigby[16] has reported that when the uterus has been altered in point of form, due to irregular contractions of its fibers causing it to be pulled down unequally to one side, while it is quite relaxed on the other side, the position of the child may be seriously affected, for it will not present obliquely as regards its long axis, and become a case of malposition. Barnes,[15] DeLee,[17] Duncan,[11] Edgar,[18] Eden and Holland,[19] Galabin and Blacker,[20] Hodge,[4] Herman,[21] Leischman[5] and Reynolds[22] have cited lateral obliquity of the uterus as one of the causes of face presentation, but no explanation is offered for the mechanism of the obliquity of the uterus. Webster[23] states that malpresentations and malpositions are apt to be produced by obliquity of the uterus, since in these conditions the long axis of the uterus is not in line with the axis of the inlet. Wigand[24] states that, "the chief cause of faulty position of the child does not depend so much upon the child itself, as upon the deviation of the uterus from its natural elliptical or pyriform shape."

There are numerous references showing that the human uterus may contract asymmetrically in its sagittal halves and the more extensive literature on contraction rings, which we do not intend to discuss in this paper, shows that the human uterus may contract irregularly in its transverse segments or portions. One of us (Rudolph) has observed two cases of marked irregular or partial contractions associated with high-grade asymmetry or sacculation of the uterus which raised the question of the mechanism of this condition in his mind. The irregularity of the contractions and tonus observed can be briefly summarized as follows: during labor it was noted that each lateral half of the uterus assumed a different form. On palpation, the tonus or firmness of the uterus was different in each lateral half of the uterus and there was a difference in the time of onset of the contractions in each lateral half, with one lateral half contracting in a normal manner and the other either not contracting or only feebly. In one case the uterus was only asymmetrical during contractions, while in the other it was continuous.

CASE 1.—Mrs. G. B., twenty-four years of age. Primipara. History, physical and prenatal examinations were of no importance. Last menstruation February 14, 1928. Expected labor November 21, 1928. Pelvic diameters: interspinal 22; intercristal 27.5 cm.; bitrochanteric 32 cm.; Baudelocque 19 cm.; biischial 9 cm.; pubococcygeal 9 cm. Examination at about the thirty-sixth week of pregnancy and on November 8, 1928. Diagnosis O.L.A., height of the uterus 32 and 33 cm., respectively, and the presenting part low in the pelvic excavation.

Onset of uterine contractions on November 11, 1928, at 11:30 P.M.; pains irregular and weak until November 12, at 3:00 A.M., when the pains became more regular and strong, every five minutes, and the patient entered the Mount Sinai Hospital at 6:00 A.M., apparently in active labor with the pains every three to five minutes and moderate.

Examination at 11:30 A.M. Diagnosis O.L.A., floating head, no effacement, and dilatation 2 cm., with pains every three minutes and moderate. Fetal

heart tones located in the left lower quadrant, and absent in the lower right quadrant, 140 and good quality. It was noticed after the patient had entered the hospital that the upper left part of the uterus would balloon out, with each uterine contraction and appeared like a cyst, about 8 cm. in diameter (Fig. 1). On palpation during a pain, the ballooned-out area was soft and no contractions could be felt; the breech occupied the ballooned-out area, and was easily palpable, while the opposite part of the uterus was contracting normally and was firm during a pain. During the pains the uterus was displaced to the left and the right border of the uterus was close to the median line of the abdomen. This condition persisted all day with slight progress and was treated expectantly. During the intervals between the pains the uterus was symmetrical (Fig. 2).

At 9:00 P.M. the ballooning of the uterus became more marked during the pains.

Examination at 11:30 P.M. Every two to three minutes there were strong pains. Bag of waters intact. Presenting part minus 3 cm., cervix effaced, and dilatation 5 cm. With each pain the ballooned area became more marked. The uterus was displaced to the left, soft, and the breech easily palpable during a pain. At this

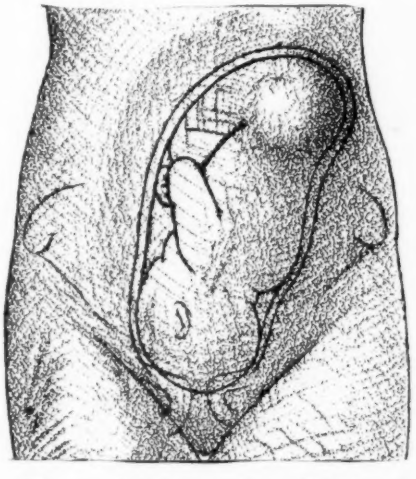

Fig. 1.—This figure is a diagram to show the cyst-like ballooning of the uterus which occurred during the pains in Case 1.

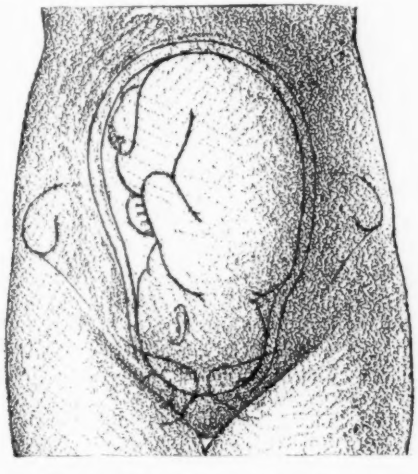

Fig. 2.—This figure is a diagram to show that the uterus in Fig. 1 became symmetrical during the intervals between the pains.

stage the problem arose as to the mechanism of this ballooning and a cesarean section was seriously considered on account of a possible rupture of the uterus through the "ballooned area."

On November 13, at 12:45 A.M., the bag of waters ruptured spontaneously during a pain, the uterus becoming symmetrical during the pains that followed. No more evidence of the ballooning area was observed and the uterus contracted during the subsequent labor pains as in a normal labor. A rectal examination was made at 12:50 A.M., the presenting part had descended into the pelvic excavation and was plus 2 cm., with dilatation of 9 cm. At 1:00 A.M., a rectal examination showed complete dilatation and retraction of the cervix, with pains every three minutes.

At 1:50 A.M., with the head beginning to crown, low forceps and episiotomy were done, and an easy delivery, with a normal third stage of labor, resulted.

The postpartum examination did not disclose any malformation of the uterus. Examination six weeks postpartum showed a normal uterus on bimanual examination.

CASE 2.—MRS. M. C., twenty-one years of age. Primipara. History, physical and prenatal examinations were of no importance, except in the last trimester the

uterus was unusually tense. Last menstruation June 28, 1928. Expected labor April 5, 1929. Pelvic diameters: interspinal 23; intercristal 25; bitrochanteric 28; Baudelocque 19; biischial 9; pubococcygeal 9. Examination at about the thirty-sixth week of pregnancy and on April 18. Diagnosis R.O.A., height of uterus 32 and 33.5 cm., respectively; the head was floating and by the Monroe-Kerr maneuver it could be pushed into the inlet with no overriding of the fetal head.

Apparent onset of labor on April 17, 1929, at 10:30 A.M., which stopped in about nine hours. On April 18, at 5:00 A.M., the pains began and the patient entered the Grant Hospital at 8:45 A.M. Until April 20, at about 1:00 A.M., the pains were very irregular, varying from slight to strong painful uterine contractions with no apparent effacement and dilatation. Diagnosis R.O.P., false labor due to uterine dysfunction, no effacement, and dilatation 1.5 cm., bag of waters intact, the head minus 3, and right lateral obliquity. On April 19, the contour of the uterus changed from a pyriform shape to a marked right lateral obliquity which persisted during

Fig. 3.—This is a roentgenogram of Case 2, which shows a right lateral obliquity which persisted during the pains and intervals for approximately forty-eight hours after which the uterus suddenly became symmetrical.

the pain and the interval. The left half of the uterus was contracting normally and approached the median line of the abdomen with firm tonus; the right half of the uterus during a pain was seen to be far to the right of the abdomen, soft, with feeble contractions. The back was easily palpable during the pains. On April 20, at 10:00 A.M., the obliquity persisted and a roentgen picture was taken (Fig. 3).

On April 21, at about 1:00 A.M., the pains became more regular, occurring at intervals of five to eight minutes, and strong. Examination at 2:45 A.M. Diagnosis O.D.T., complete effacement, and dilatation 5 cm., head plus 1 cm., uterus in the midline and symmetrical, and of equal tonus on both sides during the labor pains, bag of waters intact. At 11:30 A.M., a vaginal examination was made. Diagnosis O.D.T., sagittal suture between the left oblique and the transverse diameters, effacement complete, and dilatation 8 cm., head plus 2 cm., and the bag of waters intact. Mother in good condition and the fetal heart tones 140 and of good quality. At 11:40 A.M., the bag of waters ruptured spontaneously.

At 3:20 P.M., the head caused bulging of the perineum, and as the patient was beginning to show the strain of labor, a prophylactic forceps operation was done, in the usual manner, and the child was delivered in good condition at 3:57 P.M. Patient was returned to her room in a fair condition. Uterus well retracted and firm.

At 8:00 P.M., the patient developed a severe postpartum hemorrhage which necessitated uterine packing. Patient reacted well and was discharged from the hospital in good condition on the thirteenth day postpartum.

Shaw[25] reports a case that might be a bilateral ballooning of the fundus uteri, which occurred in a primipara, three months' pregnant, in whom a cystic tender swelling was discovered on the upper surface of the uterus and about the same size as the uterus. The swelling proved to be a thin-walled sac of the uterine wall, and its cavity communicated with the cavity of the uterus by an opening which admitted two fingers. Both the sac and uterine cavity were lined by fetal membranes and the fetus moved freely from one to the other. Bride[26] saw a similar case.

The preceding literature together with our observations of the normal and abnormal behavior of the uterus in pregnancy and labor have caused us to inquire into the coordinating mechanism of the uterus. This inquiry has led us to adopt the theory referred to in the first paragraph.

Since ontogeny recapitulates phylogeny, a comparative anatomic study of the mammalian uterus from the lowest mammalian, the Monotremes, to the highest mammalian, the Primates, will assist us in understanding the embryologic development of the uterus and will be seen to have a bearing on the problem. In the Monotremes, the uteri are not fused, and each opens into the urogenital sinus which opens into the cloaca. In the marsupials, the uteri are not fused, but just before reaching the urogenital sinus, the vaginae fuse and open almost immediately into the cloaca. In the Rodentia, the uteri are perfectly formed, each with a well-formed cervix, separated from each other, but open into a single vagina. In the Carnivora, the upper portion of the uterus is divided to form the cornua or horns, which are quite long, while the lower portions fuse into a single tube, the corpus uteri, with one cervix opening into a single vagina. In the Ruminantia, the same arrangement is found as in the Carnivora, except that the cornua or horns are much shorter.[27, 28] In the Primates, we find a complete fusion of the upper and the lower portions of the uterus, forming a single uterus with a cervix which opens into a single vagina. Fig. 4.

Embryologically all midline organs, except the urinary bladder have a bilateral origin. The human uterus is a midline organ, but has a bilateral origin. The epithelium of the uterus and genital tract comes from the two müllerian ducts, one being originally on each side of the body. The muscular and connective tissue elements of the uterus and

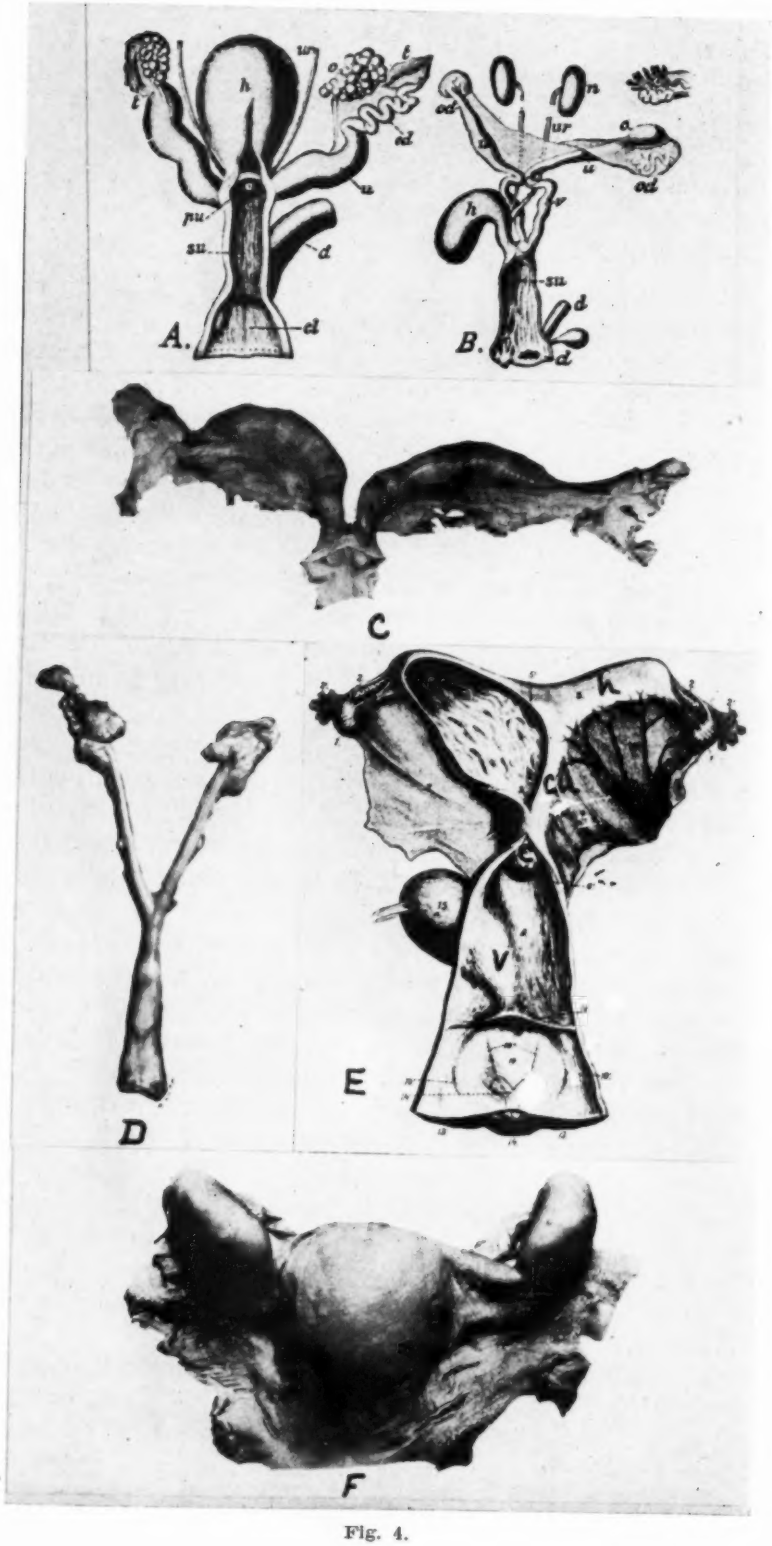

Fig. 4.

vagina come from the genital cord, which is formed by the fusion of the two urogenital folds, one from each side of the body.[29, 30, 31, 32]

The müllerian ducts begin to develop at the sixth week and arise from the outer surface of the wolffian ridge somewhat lateral and ventral to the wolffian duct. About the second month the müllerian and wolffian ducts begin to expand by invaginating the celom as a fold into the celomic cavity. This is called the urogenital fold and unites mesially with its mate on the opposite side. This fusion produces the genital cord which contains the two wolffian ducts, the two müllerian ducts, and mesenchymal elements to form muscle and connective tissue.

At about the third month fusion of the müllerian ducts occurs. After fusion has occurred, the mesial walls of the ducts disappear to form a single tube, the uterovaginal canal. Disappearance of the mesial walls of the ducts, first begins in the part that is to become the cervical portion of the uterus. The extent to which the urogenital folds and the müllerian ducts fuse varies in different animals,[29, 31] causing a greater or less degree of duplicity of the uterus. At about the fifth month the muscular walls of the uterus begin to differentiate from the mesenchymal tissue of the genital cord. Now the question of prime importance concerning the problem set out above is: Do the primitive muscle cells that come from the right urogenital fold give rise to the musculature of the right side of the uterus and those from the left give rise to the musculature of the left side of the uterus with some overlapping at the longitudinal axis; or do the primitive muscle cells from both mesenteries intermingle with and surround the müllerian ducts so that the musculature of the uterus cannot be said to be right and left sided in origin?

Embryologists do not express an opinion on this point, probably because it is of no special interest except as it bears on our problem. However, Bryce[1] and Felix in Keibel and Mall[29] state that defective fusion of the urogenital folds and the müllerian ducts explains certain malformations of the uterus seen in the human subject, but say nothing of the source of the musculature which, for example, surrounds each uterus in cases of uterus duplex in the human.

Fig. 4.—Diagrams and photographs depicting the comparative anatomy of the uterus.

A. The monotreme uterus (Echidna aculeata). The uteri open into the urogenital sinus.

B. The marsupial uterus (Didelphys dorsigera). There is a "slight" fusion of the vaginae before opening into the urogenital sinus. *SU*, urogenital sinus; *V*, vagina; *U*, uterus. (From Kingsley, Hertwig's *Manual of Zoology.*)

C. The uterus of the rabbit, uterus duplex. The rabbit has a single vagina, but a uterus on each side opening separately into the vagina.

D. The uterus of the dog, uterus bicornis; *V*, vagina; *C*, cervix; *CU*, corpus uteri; *FS*, fundal sphincter; *H*, horn. The dog has a single vagina, a lower fused portion of the uterus (the cervix and corpus uteri), and an upper nonfused portion (the horns).

E. The uterus of the mare, uterus bicornis, but the horns are relatively shorter than in the dog. *V*, vagina; *C*, cervix; *CU*, corpus uteri; *H*, horn. (From Sisson, *The Anatomy of Domestic Animals.*)

F. The uterus of the monkey (M. Rhesus). (From photograph furnished by Dr. Carl Hartman.)

Let us examine the evidence bearing on the questions asked above. According to the precept that ontogeny repeats phylogeny, it is logical to assume that the human uterus has to some extent retained its primitive physiologic and anatomic characteristics. This assumption is supported by the fact that in the human female the various types of uteri from the uterus of the Rodentia (uterus duplex) to the uterus of the Primates occur occasionally, which is obviously believed to be due to the failure of fusion of the urogenital folds and the müllerian ducts in the human embryo. In these cases in which the müllerian ducts fail to fuse, each duct receives its complement of muscular tissue from the right and left urogenital mesentery or fold, which is shown by the fact that each uterus or horn in the uterus duplex or uterus bicornis of the human being contains muscle and connective tissue. It should also be pointed out in this connection that the blood and the nerve supply of the uterus is bilateral in origin.[33] It seems logical, therefore, to assume that anatomically the greater mass of the right uterine musculature comes from the right anlage and the left from the left anlage.

There are two other points of anatomic evidence bearing on this question. First, Hofbauer[34] in describing a specialized type of muscle in the human pregnant uterus, which he believes is analogous to the Purkinje or conductive system of the heart, finds a mesial band thinning out laterally on the anterior wall of the uterus, and two thin longitudinally arranged bundles on the posterior wall. He further describes what he has seen to occur in the uterus during cesarean section after the intramuscular injection of pituitrin as follows: "A pale band from two to three inches wide, composed of parallel fibers, is visible over the anterior surface of the uterus all the way from the bladder reflexion to the fundus, in its pattern resembling the tenia of the large intestine. The wave of contraction spreads from this band and involves an ever increasing area of the pregnant organ. Synchronous with the first appearance of the tenia in the midline, there comes into view an orbicular structure surrounding the insertion of the tubes, as well as a pale zone in the midline of the posterior aspect of the lower uterine segment. These phenomena are most striking when the operation is being performed in spinal anesthesia." We have observed tenia in the rabbit and to a less extent in the dog and they would probably be more evident under spinal anesthesia, since spinal cord section in the rabbit not infrequently increases the contractions of the uterus. Second, Freund[35] diagrams in the human uterus the overlapping of circular fibers in the midline suggesting the midline overlapping of the two right and left anlagen referred to above. This is indicated, also, in the gross dissections of the uterus and in the uterus arcuatus of early pregnancy.[36] In addition to the clinical evidence cited above, Jardine[37] cites a case along with one of Professor

M. Cameron's and one of his own in which after dilatation of the cervix had occurred, there was a distinct ledge felt about three inches above the external os involving only one side of the uterus, which suggests that even contraction rings may be unilateral in occurrence.

Quite recently Hartman, Koff and Ivy,[38] observing contractions of the uterus in the pregnant monkey at term, found that the uterine contractions start near the point of insertion of the tubes, and spread mesially and then downward over the lower portion of the uterus, and they further observed in one instance that a contraction started on one side and not on the other, which caused a temporary asymmetry of the uterus.

Several physiologic facts bear directly on this question. From the standpoint of comparative physiology, it is known that contractions do not occur synchronously in both uteri in the rabbit nor in the two horns in the dog,[39] and that in the rabbit the stimulation of the right sympathetic trunk, chiefly affects the right uterus. In the uterus of the dog, we have an example of incomplete fusion of the uterine anlage, the corpus uteri being the fused portion, and the horns the nonfused portion. Physiologically, we know that in labor in the dog[39] the two horns act for the most part independently, whereas the corpus uteri acts as a coordinated whole, but is directly correlated with the activity of the horns. In the dog, then, we have exemplified incoordinated activity of one portion of the uterus (the horns) and a coordinated activity in another portion (the corpus uteri) with reciprocal coordination between the two portions (the corpus uteri and horns). Therefore, fusion of bilateral parts normally leads to a physiologic coordination in motor activity which is manifested by the normal human uterus in labor and the corpus uteri of the dog. But this does not mean that the coordination is brought about by an intermingling of the primitive muscle cells from the right and left anlage, nor by a complete overlapping of the coordinating mechanism which arises from the two anlagen. Such a process does not occur in the embryologic development of the heart. In the heart there is an auricular coordinating structure, the S-A-nodal tissue, and a ventricular coordinating structure, the A-V-nodal tissue, with a coordinating mechanism existing between the two, which when it fails, leads to heart-block and causes a partial or complete dissociation of the activity of the auricles and ventricles. The analogy drawn here between the heart and uterus is not new, since Clark[40] has previously compared the uterus and heart. A complete overlapping of the coordinating mechanism does not occur even in the urinary bladder which is a midline organ and midline in origin. The urinary bladder when it contracts normally contracts equally in both longitudinal halves, but if the right nervus erigens (n. pelvicus) is stimulated, the right side of the bladder contracts which may be followed by a contraction of the

other side. Stimulation of the right hypogastric nerve also gives a contraction which is more or less unilateral. Stimulation of the right lumbar roots gives a bilateral contraction, because there is a certain amount of crossing of fibers in the inferior mesenteric ganglion.[41, 42] So, even in the development of the bladder with its midline origin there is a bilateral mechanism for contraction with a coordinating mechanism to unify the contraction of the sagittal halves. Further, when pregnancy occurs in the human female with uterus duplex or uterus bicornis, labor and parturition have occurred. By what mechanism does it occur in such uterine malformations in the human being? Is it not quite logical, or even obvious, that the mechanism of labor in the uterus duplex of the human being is the same as it is in the Rodentia, and that the mechanism in the human uterus bicornis is the same as it is in the Carnivora or Ruminantia?

No one who has carefully observed the activity of the human or primate uterus in labor can doubt the existence of some kind of a coordinating mechanism. And our description of labor in the dog[39] has shown that a coordinating mechanism is essential. The evidence cited above of a comparative anatomic and physiologic nature strongly indicates that in the development of the human uterus a midline fusion or connection between the right and left coordinating mechanisms occurs, and we believe it must occur in order to explain the type of contractions observed in the normal human composite uterus, in which both lateral segments normally contract synchronously.

Very little is known concerning the nature of the coordinating mechanism of the uterus. It may be nervous or neurogenic, muscular or myogenic, neuromuscular or analogous to the Purkinje tissue of the heart, or hormonic, or a combination of these. That the extrinsic nerves play a rôle in the activity of the human uterus in labor is generally recognized. With the present evidence at hand it is impossible to evaluate accurately the rôle they play in the human uterus, although according to Schafer, the nerves and ganglia undergo hypertrophy along with the uterine musculature in pregnancy. In the rabbit and dog they are known to modify the activity of the pregnant uterus. For example, it is well known in the rabbit that stimulation of the hypogastric nerve or plexus usually increases the activity of the uterus, but according to our observations[39] their section does not fundamentally interfere with labor; whereas in the dog we have been unable to demonstrate an effect on stimulating the extrinsic nerves of the uterus[39] but on section of the pelvic nerve, pregnancy is prolonged and in some cases incomplete because of disturbance in the activity of the vagina.[39] However, Goltz and Ewald[43] and others observed successful labor in a dog with complete destruction of the spinal cord below the lower thoracic segments which shows that the uterus is as fundamentally automatic in nature as the heart, stomach, bladder, and

rectum. The possibility of reflexes of a coordinating nature through the inferior mesenteric ganglion must be considered, but Kabierski and Heidenhain[44] and Masius[45] found that parturition occurred after section of the nerves to the uterus in dogs. A nervous reflex mechanism from the cervical ganglia must be considered, but Rein[46] removed the cervical ganglia in a dog which later gave birth to a litter, a fact which we have confirmed in two dogs (labor was abnormal in our dogs). Fleming[47] recently presented evidence of the existence of an intrinsic nervous mechanism in the uterus. He found a network of nerve fibers in the uterine wall, but no nerve cells comparable to those in the sympathetic ganglia. But he believes as a result of his histologic work and the action of drugs that there is "some arrangement for the control of tone and movement distributed at different levels." Although a hormone, or hormones, may be concerned in the initiation of labor, and are undoubtedly concerned in the uterine hypertrophy of pregnancy, it is unlikely that they are concerned in the causation of the coordinated activity of the uterus in labor. The most reasonable theory, then, of the nature of the coordinating mechanism is that it is either myogenic or neuromyogenic. The work of Hofbauer[34] supports the latter theory in that he finds histologic evidence of the existence of fibers in the uterus analogous to the Purkinje fibers of the heart.

EXPERIMENTAL

In a previous article[39] we have described a method for recording contractions of the postpartum uterus of the dog. By using this method it was found that most of the movements were initiated in the upper portion of the horn and traveled downward to the corpus uteri (in the absence of local irritation), or in other words, the contraction of the horns was usually followed by a contraction of the corpus. This type of polarity of the uterus has also been found to be present in the human vagina by Templeton, Stein and Schochet.[48] It occurred to us that by using this phenomenon, we might be able to study the coordinating mechanism of the uterus. We could by section separate the horns from the corpus and ascertain whether or not the polarity phenomenon persisted; and also excise the uterovaginal ganglia and ascertain whether or not the polarity phenomenon persisted.

METHOD

A balloon was placed in either one or both horns and in the corpus uteri of dogs from eighteen to seventy-two hours postpartum. The record of normal contractions was obtained; then each horn was separated from the corpus and a record obtained; and then the uterovaginal ganglia were excised and a record was obtained. In some experiments the ganglia were excised prior to the separation of the horns. The necessary operative work can be done without disturbing

the blood supply of the uterus. Experiments have been performed so far on seven dogs. It is not difficult to find and excise the ganglia, because they are markedly hypertrophied by pregnancy.

RESULTS

Our detailed observations will be published elsewhere, and will only be briefly summarized in this article.

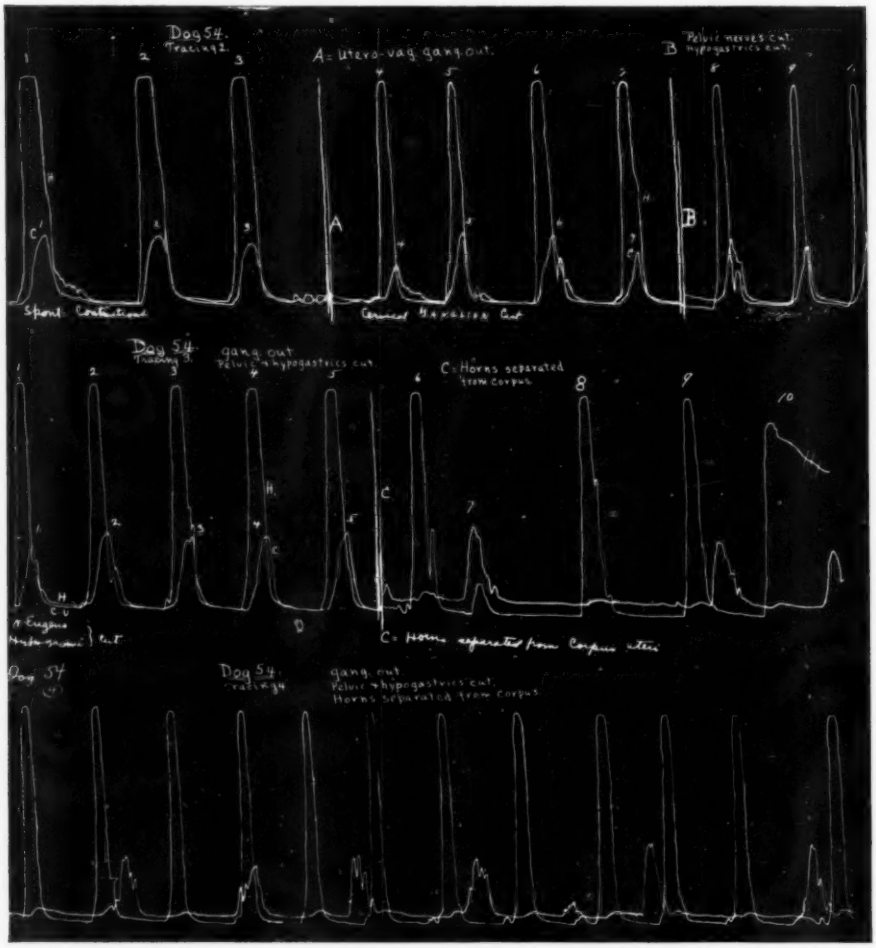

Fig. 5.—The figure shows the effect of first separating the horns from the corpus uteri, which caused no disturbance in correlated activity between horn and corpus, and then on removing the uterovaginal ganglia, which caused a dissociation of contractions of the horn and corpus uteri. (Dog 54.)

We found that when both horns contracted simultaneously, a single contraction of the corpus would follow. When one horn contracted and was then followed shortly by the contraction of the other, a summation, or superposition effect was manifested by the corpus. When one horn contracted and was then followed a minute or so later by the

contraction of the other, a double contraction of the corpus would result. In other words, the musculature of the corpus manifested the phenomenon of refractory period and summation, or superposition with reference to the propagated message or excitatory impulse.

Occasionally we observed a contraction to occur in, we will say, the left horn which would be followed by a contraction of the corpus, and then the region of the right fundal sphincter would contract which was followed by a contraction of the right horn, giving the appearance of a reversed contraction of the right horn.

As a rule when one horn was separated from the corpus, after a preliminary period during which coordinated activity or polarity was disturbed, the corpus would only contract after the remaining horn contracted, which indicated that the separated horn was no longer affecting the activity of the corpus.

When we separated the other horn from the corpus, after a preliminary period of irregular activity varying from five to thirty minutes, coordination between the separated horn and corpus would be reestablished. Now, on exision of the uterovaginal ganglia, the coordinated activity would disappear and would not reappear during a succeeding period of one hour. We have found that it is necessary to remove the ganglia completely. (Fig. 5.)

If the uterovaginal ganglia were first removed, disturbance of coordination would not result, provided care was exercised in removing the ganglia, but on separation of the horn from the corpus dissociation of horn and corpus resulted.

Hence, it is evident that the coordinated type of activity of the dog's uterus we have studied can be controlled by either of two mechanisms: one in the wall of the uterus and the other mediated by the uterovaginal ganglia; and that either mechanism in the absence of the other can carry on this coordinated activity of the dog's postpartum uterus.

Even after the removal of the ganglia and the separation of the horns, the uterus continues to contract, but there is no coordination of these contractions. However, the corpus is definitely affected by the removal of the uterovaginal ganglia. It becomes quite relaxed as a rule, its contractions are not as strong, and one observes frequently, which is shown on our tracings, irregular, feeble contractions of different muscle groups, resembling fibrillations. This observation is interesting in the light of Rucker's[49] report that sacral anesthesia causes marked relaxation of the lower uterine segment and an increase in the tone of the fundus. The obstetric literature on this point, however, is rather chaotic.[50-57]

SUMMARY OF EXPERIMENTS

These observations show that there is an intrinsic and an extrinsic coordinating mechanism in the dog's uterus and that one may sub-

serve, in part at least, the function of the other. In what layer of the uterine wall most of the intrinsic coordinating mechanism lies has yet to be determined.

DISCUSSION

A failure of the coordinating mechanism of the uterus, then, would lead to dissociated irregular or partial contractions of the uterus depending on the degree and portion of the coordinating mechanism affected. A block of the coordinating mechanism between the right and

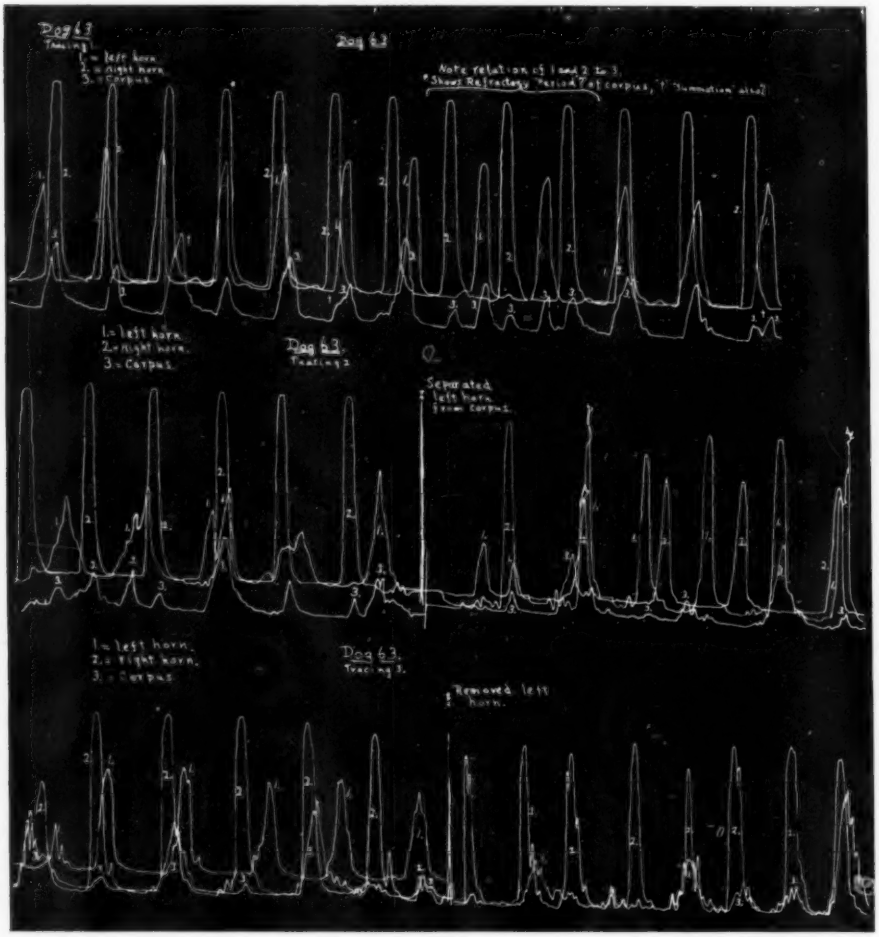

Fig. 6.—This figure shows several interesting features. Records of contractions were made from both horns and the corpus uteri. In Tracing 1, it is to be noted that when the two horns contracted together only one contraction of the corpus resulted; when they contracted a little farther apart, the corpus a "notched" or double contraction; and when they contracted still farther apart, the corpus contracted just after each contraction of the horn. The first part of Tracing 2 shows the same phenomena. This demonstrates refractory period and summation or superposition. In Tracing 2, the left horn was separated from the corpus, resulting in some disturbance of coordination between left horn and corpus. In Tracing 3, the left horn was completely removed from the body of the animal, and it is to be noted in this tracing and the first part of Tracing 4 that right horn contracts in a coordinated manner with the corpus. In Tracing 4 the right horn was separated from the corpus and a disturbance of coordination resulted, which is not as marked as that which occurred in Tracing 6 and Tracing 7 after removal of the uterovaginal ganglia.

left halves would lead to an absence of a synchronous time of onset of the contraction in the two halves. A slow conduction in one-half compared to the other half would lead to more rapid contraction on the normal side with a slow spreading contraction on the affected side, similar to the cases described by DeLee and others referred to previously. An absence or a functional defect of the mechanism in one-half would cause an absence of contractions in that half, and give rise to the condition of, or a condition simulating obliquity of the uterus.

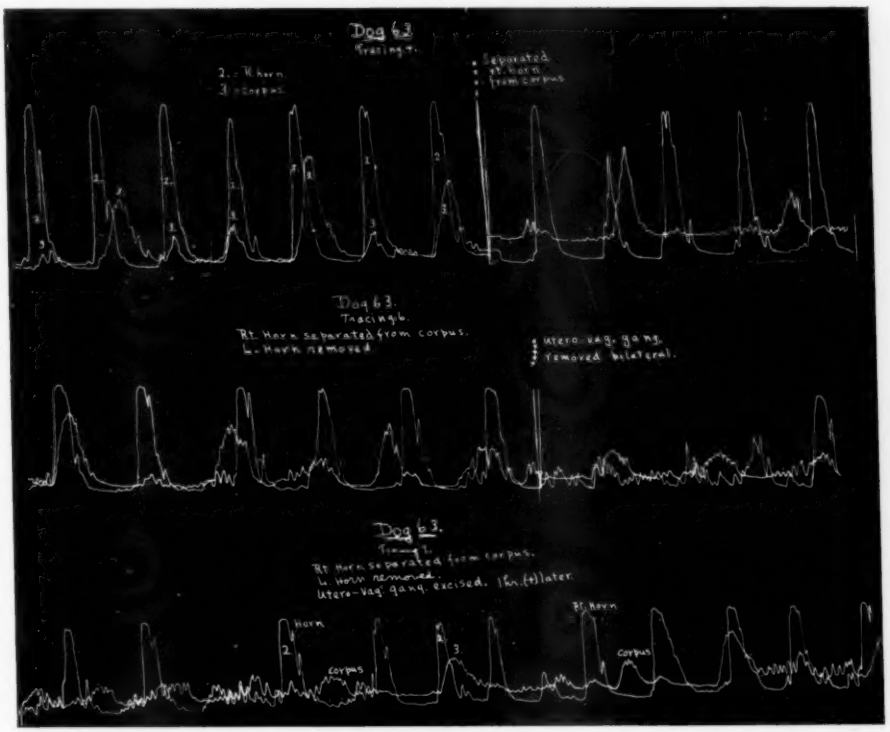

Fig. 6. Cont'd.

A failure of the coordinating mechanism in one-half, however, will not explain the asymmetry of the uterus in early pregnancy. DeLee[68] cites different types of asymmetry of the uterus in early pregnancy in which the musulature of one side manifests more hypertrophy than the other. This condition we believe is best explained by a defect in the musculature of the affected side which renders it slow in responding to the hormonal influence responsible for causing uterine hypertrophy. On the basis of the bilateral origin of the anlage of the uterine musculature such a defect (unilateral aplasia) is not unlikely and is comparable to some of the cases of uterus duplex or bicornis in which one uterus or horn has a greater complement of muscle than the other.

On the basis of a defect in the coordinating mechanism, the observed facts occurring in our Case 1 may be explained as follows: In this case there was in addition to the obliquity, a cyst-like ballooning of the upper left quadrant during pains with the result that during a contraction the breech moved up into the ballooned or noncontracting portion, and the head moved up and out of the pelvis; but on rupture of the membranes, the contractions of the uterus became normal and birth resulted. The cyst-like ballooning, we believe, was due to a greater degree of functional paralysis or paresis of the coordinating mechanism in the region of the uterus corresponding to the location of the orbicular muscles of Ruysch; and on rupture of the membranes, some factor operated to remove the functional defect. In Case 2, after a prolonged period of inertia, the contractions occurred synchronously on both sides, but were much stronger on one side than on the other, which caused an obliquity during contractions, but at a later period became of equal intensity on both sides. The fact that the contractions finally became symmetrical shows that there was no fundamental defect in the capacity of the muscle to contract. The factor causing the inertia must have affected the two halves of the uterus unequally, so that the side in which normal contractions recurred last, was the most affected, resulting in either defective conduction in the coordinating mechanism or a decreased irritability of the uterine musculature. The causative agent could not have primarily acted by way of the blood because then both halves of the uterus would have been equally affected.

Other types of asymmetrical contractions or dilatations of the uterus, such as those described by Bar,[8] DeLee,[17] Kerr,[9] Soleri[13] and others in which isolated contractions or dilatations occur at the uterine angles in the absence of an anatomic defect, and such as the various types of transverse contraction rings, can be explained as ectopic contractions or dilatations of the uterus, which may be analogous to the ectopic contractions that occur in the heart and to local circular spasms that are known to occur in the stomach, esophagus, and colon. On the basis of comparative anatomy and physiology we suggest that the so-called "ring of Bandl" is analogous to the fundal sphincters of the dog, which lie at the junction of the horn and corpus uteri.

Hofbauer[34] explains the condition of placental site paralysis or paresis by pointing out that hemorrhage may cause separation or dissociation of the fibers which he believes constitute the conducting and coordinating system of the uterus. He further points out that defective development of the specialized system he describes was observed in a specimen obtained from an elderly primipara in which inertia uteri occurred. In our two cases, however, the system must have been present but only temporarily functionally deranged, since normal contractions were observed to occur, which after they made their appearance resulted in the effacement and dilatation of the cervix in both cases.

Our previous observations on the dog and rabbit[39] show that the placental site is less active or motile than the remainder of the uterus which indicates that the placenta exercises in some way an inhibitory action on the local coordinating mechanism or muscle fibers. In the dog the placenta is only completely separated by a marked longitudinal contraction plus a circular contraction after the pup is born. This means that the expulsion of the fetus either releases the placental site from inhibition or sets up a more intense stimulation which breaks through the inhibition. The relative inertia of the placental site during uterine contractions is also true of the uterus of the monkey according to the observations of Hartman, Koff and Ivy.[38] (This discussion is not to be interpreted as depreciating the rôle that the retroplacental hematoma may play in the separation of the placenta.)

This paper has raised a number of questions—one that is of obvious particular interest is: In what percentage of cases do the uterine contractions occur asynchronously and asymmetrically in the two lateral halves of the uterus in the early period of the first stage of labor and may this factor play a rôle in determining the position of the presenting part?

SUMMARY

In this paper two cases of asymmetrical contractions of the uterus in labor are reported. These cases raised the question of the mechanism concerned. A review of the embryology, comparative anatomy, and physiology of the uterus shows that it has a bilateral origin and that the two halves except where fused act more or less independently. On fusion a correlating mechanism becomes manifest.

A type of coordinated activity manifested by the postpartum uterus of the dog has been studied. An extrinsic and intrinsic mechanism has been discovered, one resident in the uterine wall and the other in the uterovaginal ganglia, the former being the most important; and it has been found that the dog's uterine motor mechanism in situ manifests the phenomena of refractory period and "summation." On the basis of a functionally defective coordinating mechanism, the irregularity in the uterine motility, obliquity of the uterus, in the two cases observed, is explained and a basis for the explanation of other types of abnormal motor activity is offered.

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(For discussion, see page 141.)

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RHABDOMYOSARCOMA OF THE CORPUS UTERI

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INTRODUCTION

SARCOMAS of the uterus are quite infrequent. Altogether they comprise less than 1 per cent of all uterine tumors. The danger of sarcoma in a myomatous uterus is estimated by various authors, usually at from 0.6 to 1.8 per cent (see Schreiner,[1] Berreiter,[2] Evans,[3] Kunez,[4] Imhaeuser[5]). They occur most commonly within the myometrium, and at times apparently within preexisting myomas (Albrecht[6]). Submucosal tumors are less frequent, and subserous ones are quite rare indeed.

Sarcomas of the uterus are usually composed of homologous tissue. There may be very immature and indifferent elements, the round or spindle cell sarcoma, or less immature and better differentiated cells, the fibro- or leiomyosarcoma, or mixtures of both in all possible combination. All these tumors have cellular prototypes in the normal constituents of the uterine wall. But tumors composed of tissue which is foreign to the uterus may also occur.

Heterologous tumors are less frequent than the homologous ones. Lahm[7] collected altogether 50 cases from the literature. They may be simple or complex, and either benign or malignant. Among the simple tumors, lipomas are most common, but chondromas, osteomas, myxomas, and neurofibromas also occur. The complex tumors may contain various combinations of these elements, together with smooth and striated muscle cells and glandular structures of all kinds (Frank[8]).

The heterologous tumors occur almost anywhere in the uterus, but are usually submucosal (Gerich[9]). This location is particularly characteristic of the mixed cell types, which appear almost always as polypoid masses hanging into the cavity of the uterus from a broad submucosal base. Intramurally, these tumors are rare, subserous ones even more infrequent (Schroeder[10]). Except for the lipomas which occur usually in the corpus, heterologous tumors elect the cervix much more frequently than they do the corpus uteri (Jones,[11] Wiener,[12] Gustav[13]). Gamper[14] collected from the literature, only 18 of them in the corpus uteri, and these were almost all submucosal, conforming to the type of sarcoma botryoides seen in the vagina in children and in the cervix in younger adults.

A few of the heterologous tumors of the uterus contain striated muscle. It was found in 18 of the 50 cases collected (Peterson[15]). It was present in only 6 of the corpus tumors reported (Shaw[16]). But

whenever striated muscle cells do appear in the uterus, they do so almost always in association with the complex, submucosal, botryoid forms (see Fels,[17] Reeb,[18] Glynn[19]). Rarely indeed do they appear as simple rhabdomyomas or rhabdomyosarcomas.

The following case is reported because it multiplied rarity of circumstance in that a heterologous tumor composed of malignant, embryonic striated muscle cells, was found unassociated with other sarcomatous elements, located in the corpus rather than in the cervix, in the subserosa rather than in the submucosa, and had apparently started in a preexisting myoma.

CASE REPORT

A white woman, fifty-two years old, with no history of any menstrual disturbance. The menses had begun at sixteen. She had borne two, normal, full-term children. The menopause had occurred at thirty years, and there had been no bleeding since.

Twelve years ago she had had an attack of pain in the lower abdomen, and was then told by a physician that she had a "fibroid" tumor in the pelvis. It bothered her no more, however, until just two months before her admission, when she began to suffer again from dull pains in the lower abdomen. She complained also of nausea and a marked weakness, and lost rapidly in weight.

After a short rest she felt better and was up and around until two weeks before entrance when the pains recurred. She began to feel feverish and took to bed. In the last week, she had become delirious.

Physical Examination.—She was markedly emaciated. She lay in bed acutely ill, semicomatose and in muttering delirium. Her temperature was 102°, her respiratory rate 36, her pulse 160. Heart and lung findings were negative. In the abdomen, a grapefruit-sized mass was felt rising high above the symphysis. It was soft, round, regular, somewhat tender to palpation and immobile. It filled the pelvis, and obliterated the vaginal fornices. A definite corpus uteri could not be distinguished in the mass. The cervix could not be palpated. Speculum examination showed nothing. She died in less than 24 hours after entrance into the hospital.

Clinical Diagnosis was.—Carcinoma of the corpus uteri, with inflammation, degeneration or pyometra, or degenerating fibromyoma.

Abstract of Necropsy Findings.—There was a focal bronchopneumonia in both lower pulmonary lobes with hypostasis, and a septic softening of the spleen. There were also a brown atrophy and parenchymatous degeneration of the myocardium and liver, a nodose goiter and a slight arteriosclerosis of the kidneys. The essential pathologic findings, however, were in the pelvic organs.

The uterus was transformed into a large, globular, irregular mass 18 × 14 × 8.5 cm. in diameter. The vaginal fornices were obliterated. The cervix was elongated and compressed and opened abruptly into the apex of the narrow vaginal vault. From the external os hung a narrow, pedunculated polyp 9 mm. in diameter. Its stalk was 1.5 cm. long and 3 mm. in diameter. Surfaces made by section revealed the cavum uteri to be compressed into the right lateral portion of the large, uterine mass. The cavum was 9 cm. long, 3 cm. in anteroposterior and only 1 cm. in transverse diameter. Within it, hanging from the left cornu, there was a second, smaller, fibromyomatous polyp.

The large irregular mass described was 12.5 cm. in greatest diameter. It was incorporated within the left lateral wall of the uterus, and had expanded it. Centrally it was homogeneously purplish-red. Toward the periphery it was more edematous and yellowish-grey. Between this large, intramural mass and the left

ovary, another, more boggy mass, 8 cm. in diameter, was interposed. It arose subserously from the left cornu. It was quite friable. Surfaces made by section were centrally purplish-red, peripherally were mottled with pearly-white areas, dull reddish-grey and yellowish mucoid ones.

The left fallopian tube stretched anteriorly over the crest of this mass for a length of 12 cm. to reach its ovary. The left ovary was edematous, soft and swollen to 6 × 4 × 3 cm. in diameter. The right fallopian tube was grossly normal. The right ovary contained several small and a few larger cysts up to 15 mm. in diameter, filled by clear fluid.

Microscopic Examination.—Sections from the pearly-white areas in the subserous node showed a marked cellular pleomorphism, but cells of elongated shape predominated. The latter cells were sometimes drawn out into long bands. There were also many huge, round or oval cells. In all, the nuclei were either single or multiple, of irregular shape, and rich in chromatin. The chromatin usually formed coarse granules, and there were one or two large, round nucleoli.

In the huge cells, the cytoplasm was deeply eosinophilic. It was often gathered in the center about the nucleus, and only protoplasmic, spider-like processes of it

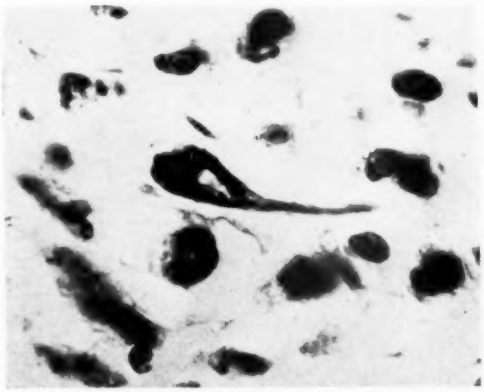

Fig. 1.—Well differentiated cross striation in the elongated cell in the center of the field. Scattered centriole granules and abortive fibril formation in the other cells. Mallory's phosphotungstic acid hemotoxylin. ×1200.

extended to the cell membrane in the periphery. The remaining part of these cells appeared empty, and vacuolated. They sometimes contained hyaline droplets which stained bright red with eosin, and orange red or deep blue with Mallory's phosphotungstic acid hemotoxylin. In the band shaped cells, one end was frequently thickened, club shaped, and contained the nucleus. In others, a long nucleus extended through the entire length of the cell; in still others several nuclei were crowded together.

With Mallory's phosphotungstic acid hemotoxylin, fine deeply staining purplish-blue granules of varying size, and clusters of these granules were seen in many of the cells, quite close to the nucleus. In others they were found scattered throughout the cytoplasm, and even in the protoplasmic spider-like processes. From many of the scattered granules, a tapering fibril extended in both directions. The granulated fibrils usually appeared singly and in no orderly arrangement. Occasionally they were lined up in small bundles, in the cytoplasm, or in the form of fine, longitudinal fibrils. After long searching, a distinct cross striation could be detected in a few of the cells. A sarcolemma was absent, or when present was poorly defined.

Between the cells were found fine fibrils of collagenous tissue. There were many capillary blood vessels which were often filled by a fine net of fibrin. Large vessels contained more compact, hyaline masses of fibrin. The greater part of the tumor was completely necrotic, so that no structure at all could be defined.

Sections from the intramural mass showed only the structure of a simple fibromyoma with advanced degenerative changes, hemorrhages and necrosis, but no evidence of malignancy.

Anatomic Diagnosis was.—Very immature rhabdomyosarcoma of the uterus, originating subserously from the left cornu; intramural fibromyoma in the left lateral wall of the uterus with red degeneration; displacement of the corpus uteri, compression of the cavum uteri and elongation of the left fallopian tube by the intramural fibromyoma; pedunculated fibromyomatous polyps of the corpus and cervix uteri, and serous and follicular cysts of the right ovary, and edematous swelling of the left.

DISCUSSION

The rhabdomyosarcoma was found associated with multiple fibromyomas. Leiomyosarcomas have been frequently reported in such association. The same uterus may contain a myoma and a sarcoma which are entirely independent of each other (Newell[20]). A sarcoma may develop just outside a myoma, invade and completely destroy it. More frequently, however, a sarcoma may develop within a myoma, and completely replace its benign predecessor (Dannreuther[21]). In 46 cases of leiomyosarcoma of the uterus, Frankl[22] found 22 developing on the basis of a myoma. On the other hand, one can never be sure in these cases that the compound tumor had not begun as a sarcoma which subsequently slowed down in certain parts to differentiate mature smooth muscle elements. Sage,[23] von Kuettner,[24] Ulesco-Stroganowa[25] and others hold that sarcomas frequently begin in preexisting myomas. Ewing[26] admits that they may do so, but believes that most of them are malignant from the first. A preexistent myoma may be indicated by:

1. Definite encapsulation of the tumor.
2. Retention of old calcified portions of myoma in the periphery of the mass.
3. Presence of other fibromyomas.
4. History of old fibromyomas.
5. Marked change of shape of the uterus, distortion of its cavity and hypertrophy of its walls, just as these appear in any simple fibromyoma of large dimensions and long existence (Kaufmann[27]).

Most of the heterologous tumors of the uterus do not arise in association with myomas, but exceptionally they may do so (Ritter[28]). The tumor in my case was definitely encapsulated. Yet a slowly, expansively growing tumor may too assume a sort of capsule. There were no calcified remnants of an old fibromyoma present, but most of the sarcomatous mass had undergone such necrotic changes that it was impossible to discern what had been there before. Even could mature fibromyomatous tissue be demonstrated directly within the malignant node, it would still be possible for it to have developed to-

gether with, or after the sarcomatous elements, but at a slower tempo.

The possibility that the subserous, sarcomatous mass was a recent and independent development cannot be precluded. But there was a definite history of multiple, large fibromyomas known to have been present for at least twelve years. There were other fibromyomas present, and these had undergone red degeneration and necrotic changes similar to those of the sarcomatous mass. The uterus showed the hypertrophic changes and distortion which comes with large, long-standing tumors. It is certain that multiple fibromyomas had long been present in this uterus. It is at least likely that the rhabdomyosarcoma had begun in one of them.

That a striated muscle tumor should appear in the uterus, indeed in a myoma uteri, is odd. Orthotopic rhabdomyomas occur in the heart, in skeletal muscle, in the tongue, wherever striated muscle cells are ordinarily present (Dewey[29]). In the uterus, striated muscle cells are not normally present. Yet in it, rhabdomyomas may occur. In fact, it is the more frequent site for ectopic rhabdomyomas.

Marchand[30] and Ribbert[13] maintained that they arose here, by metaplasia from the smooth muscle cells. It is not conceived that mature smooth muscle elements can degenerate into neoplastic striated muscle cells; one should therefore not speak of a sarcomatous degeneration. But among the differentiated cells of almost every tissue, there are rests of very immature, homologous and indifferent cells. These are available as sources for constant replacement, for regeneration after injury, and according to Cohnheim[32] for the proliferation of tumors. It is from such immature cells that myomas develop and from the remaining, still more immature but latent rests that a homologous sarcoma of any kind may secondarily, in abruptly faster tempo, develop within a myoma. It is then held that these very immature anlages of smooth muscle cells can alter their usual course of differentiation and produce striated muscle tumors.

Metaplasia can account for the development of smooth muscle, cartilage and even bone from a mesenchymal stroma. But it is quite unlikely that such a process can account for the production of striated muscle fibers, and particularly for a neoplastic proliferation thereof (Gamper,[14] Hauser,[33] Gordon[34]). In embryonic origin, smooth muscle and striated muscle are derived from sources too widely separated, for one type to transform itself into the other. Smooth muscle is derived from indifferent mesenchyme syncitium, striated muscle from the mesodermal somites. Much of the difficulty has arisen from the resemblance of undifferentiated striated muscle cells to smooth muscle cells. They may be growing side by side. But, they belong to different groups and the apparent transitions between the two are only due to the difficulty in distinguishing the younger forms.

Most investigators at present (Kolisko, Kehrer[35]) deny this metaplasia, but attribute the heterotopic striated muscle tumors to the

embryonic displacement of anlages of striated muscle cells. Similarly they ascribe the mixed tumors to displacements of embryonic mesoderm which can then differentiate both striated muscle cells and mesenchymal elements such as smooth muscle, cartilage, fat, elastic tissue, etc. That they are derived from teratomas, inclusios foetus, in which striated muscle cells predominate is denied, because true embryonic endodermal or ectodermal structures have never been satisfactorily demonstrated in them (see Mackenzie,[36] Cox,[37] Himwich[38]).

The genital tract has a very complicated development, and embryonic displacements can readily occur. The primary excretory duct of this system, the wolffian duct, grows down from the thoracic segments. The müllerian ducts develop just laterally to them, then swing in under them from each side to reach and fuse in the midline to form the uterus and vagina. In the female, the wolffian ducts then disappear, or only vestigial remnants persist as Gärtner's ducts. But when these ducts are complete, they pass from the epoophoron through the broad ligament at first parallel to the fallopian tubes. Then they pass diagonally into the uterine substance approaching the mucosa and even extending in the lateral wall of the vagina to the hymen (Wilms,[39] Keibel and Mall,[40] Fischel[41]). This course of the wolffian duct marks the line of location of the heterologous tumors as they are found in the female uterus and adnexa.

It is therefore held that embryonic mesodermal cells from the myotomes of the dorsal region become attached to the wolffian duct, and are carried down with it in its caudal growth toward the vesicourethral anlage. They are dropped anywhere along its course in the adnexa, the corpus, the cervix, or the vagina. For years they remain dormant. In later life, under the stimulus of an infection, an irritation, adjacent tumors, constitutional predisposition, etc., these rests proliferate to form the heterologous tumors. From indifferent mesodermol round cells, a variety of mesenchymal structures may differentiate. From the myotome cells, striated muscle cells develop. But these stimuli would never produce the heterologous growths if the direct anlages of such cells were not already present (see Meyer,[42] McLean,[43] Barris[44]).

Striated muscle tissue has indeed been found incidentally in the uterus, even without tumor formation. Girode[45] and Nehrkorn[46] ran across islands of fully differentiated striated muscle cells in two uteri removed after puerperal sepsis. Nehrkorn found in his case evidence of an old perimetritis, Lahm[7] also found in adult uteri sheets of cells between the endo- and myometrium resembling embryonic striated muscle. Under pathologic irritation, these could well serve as the basis for the development of rhabdomyomatous tumors.

At various times, striated muscle cells have also been described as constituents of myomas. Ewing in fact accepts the ordinary myoma as resulting from an embryogenic disturbance in the development of

the uterus. Displaced striated muslce anlages are occasionally caught up in them, and by subsequent proliferation produce rhabdomyomas or even rhabdomyosarcomas within the preexisting myoma. But these anlages and their tumors may just as well, however, appear independently or alone.

Not always in striated muscle tumors can cross striation be demonstrated. The more immature the tumor, the more difficult is this to do. It was only after long searching that an occasional cross striated fiber could be found in this case. But the histologic diagnosis should be suggested, and can be established without them. Attention was called to the true nature of this tumor by the large cells with vesicular and often multiple nuclei, centrally placed within the deeply eosinophilic, finely granular, and often vacuolated cytoplasm which extended in spider-like threads to the periphery of the cells. They resembled embryonic myoblasts, and at times were fused into cell cylinders. The granules about the nucleus were clusters of paired centrioles. These, according to Wolbach,[47, 48] are scattered into the cytoplasm and acquire short tapering fibrils at each end. Mallory's phosphotungstic acid hemotoxylin demonstrates these structures best. The granulated fibrils multiply rapidly and finally line up into fully differentiated striated cells. But even in the absence of definite cross striation, these tumors of myoblastic origin may be identified by the large cells just described, and established by the presence of their centriole clusters and abortive fibril formation.

The histologic distinction of a rhabdomyosarcoma from a leiomyosarcoma and a fibrosarcoma is of more than academic importance. Fibrosarcomas are extremely malignant, giving rise quickly to widespread, massive, hematogenous metastases. Leiomyosarcomas are far less malignant, and may be successfully extirpated with some prospect of cure. Rhabdomyosarcomas are slow to metastasize but they will recur promptly after an extirpation. They offer a grave prognosis because of their rapid growth, extensive local infiltration, pressure effects and degenerative changes (Halter,[49] Hamrick[50]). Death occurs in these cases almost always in less than one and a half years after the onset of symptoms.

The clinical distinction of rhabdomyosarcoma from other types of sarcoma is impossible preoperatively, except for the submucous botryoid types which may be diagnosed from curettage specimens or from spontaneously extruded necrotic pieces of tumor (cases of Sternberg,[51] Bunten[52]). It is difficult enough to diagnose the development of any sarcoma, particularly when it is associated with fibromyomas. In these cases, the preoperative histories are almost identical with those of ordinary fibromyoma cases. There is nothing in the history or physical examination which makes it possible to suspect malignant transformation until cachexia, anemia and emaciation announce an

irremediable state. These corpus sarcomas appear characteristically, however, after the menopause, when myomas should tend to regress. Should fibromyomas begin to enlarge after the menopause, should intractable pain independent of the menses appear, should loss of weight, anemia or a septic process become manifest, the diagnosis of sarcomatous transformation may at least be suggested.

SUMMARY AND CONCLUSIONS

A rare case of rhabdomyosarcoma of the corpus uteri is reported. It arose subserously, as a simple heterologous tumor, and apparently within a preexisting myoma. It developed from embryonic rests of striated muscle cells displaced in the course of the downgrowth of the wolffian duct.

These tumors may be identified histologically even in the absence of definitely cross striated cells. They present large cells with central nuclei, and deeply eosinophilic, often vacuolated cytoplasm which extends in spider-like processes toward the cell membrane. Centriole clusters can be found around the nucleus, and abortive, granulated fibril formation throughout the cells.

The distinction from a leiomyosarcoma and a fibrosarcoma is important because of the differences in degree and manifestation of malignancy. The clinical diagnosis is often obscured by the presence of preexistent fibromyomas, so that sarcomatous transformation is suspected only when it is irremediably far advanced.

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KRUKENBERG TUMORS OF THE OVARY

With Report of a Case Secondary to Adenocarcinoma of the Jejunum

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RECENT literature has contained reports of bilateral ovarian neoplasms containing both fibrous and epithelial elements which are usually found in association with malignant disease of the gastrointestinal tract. The relative rarity of these tumors, however, seems to justify the addition to the literature of this case of bilateral Krukenberg tumors associated with adenocarcinoma of the jejunum. The lesion was originally described by Friedrich Krukenberg in 1895 as a bilateral ovarian tumor of slow growth which caused general and somewhat symmetrical enlargement of the ovaries but preserved the regularity of their general contour. Krukenberg studied the histology in detail and called the tumor fibrosarcoma ovarii mucocellulare (carcinomatodes). Although there is some evidence that occasionally tumors of this type are primary in origin, the majority of cases are in association with carcinomas of the stomach and have been assumed to occur either by a direct implantation into the ovaries or by retrograde lymph flow.

Fallas, in reviewing the literature, has been able to collect 55 cases prior to 1918 and has added 23. The primary neoplasm has been, almost invariably, in the stomach. Ewing believes all of these tumors are secondary and that failure to find the primary growth does not mean that such lesions did not exist. Histologically, this tumor, originally called fibrosarcoma, is made up of a cellular fibromatous network dotted with large vesicular cells of the mucoid type, the nucleus

of which is often pressed against the cell boundary. This eccentric displacement of nucleus has given rise to the name "signet ring" cells, which are considered characteristic of the tumor. Certain tumors show large mucoid areas of softening as well as areas where the gland-like arrangement is well preserved. In other places (see Fig. 4) the adenoid arrangement has been practically lost and the appearance is that of a somewhat loose but richly cellular connective tissue network in which are scattered singly and in groups typical large bright cells, some of which are seen to be of the "signet ring" variety. As has been pointed out, it is generally admitted that these tumors are most commonly metastatic from scirrhous carcinomas of the stomach, and secondary carcinoma of the ovary metastatic from carcinoma of the jejunum, is extremely rare (Roblee).

CASE REPORT

The patient was a nurse aged forty-eight, para 0, white, weighing one hundred pounds, admitted January 12, 1929 to the medical service complaining of general malaise, loss of appetite, frequent vomiting, and severe pain in the lower left quadrant. These symptoms began November, 1928 and gradually increased in severity. Since then, nausea, vomiting, increasing pains in the lower left quadrant and in the rectum, and considerable distension of the abdomen have occurred with increasing frequency and severity. She gave a history of chronic constipation for years and was relieved only by oil enemas during the past fourteen weeks. She had lost thirty pounds in weight in the last year and had become anemic and weak.

Menstrual history was negative except that the intermenstrual periods had become longer during the past year and the flow less in amount. Physical examination showed a white, very nervous, thin woman in no great pain, pallid, with wrinkled skin. Mouth, teeth, heart, and lungs were normal. The abdomen showed considerable relaxation of abdominal wall and moderate distension of cecum and tenderness in the lower left quadrant. There were no adenopathies.

Pelvic examination was unsatisfactory because of senile retraction and of extreme tenderness in the vagina. There was considerable leucorrhea. Examination under anesthesia on June 15, 1929 revealed a senile atrophy of the vagina and cervix. The uterus was anterior and fixed. There was a large ovarian mass to the right and a similar, slightly elongated mass to the left which extended up along the left broad ligament region. These masses were only slightly movable. Rectal examination disclosed two to three small nodules one and one-half to two cm. in diameter in the rectovaginal wall. Proctoscopic examination was negative.

Laboratory Findings: Barium enema June 18, 1929 was negative. Urine was normal. Blood 8500 W.B.C. R.B.C. 3,300,000. Hb. 40 per cent. Blood smear showed anisocytosis and poikilocytosis and some polychromatophilia. Color index 0.6. Blood Wassermann negative. Blood grouping Jansky two. The patient was operated upon on June 21, 1929 after a transfusion of 500 c.c. of blood. A dilatation and curettage was done and a small amount of curettings was obtained. A low midline incision was made and the gall bladder was found enlarged but it emptied readily. There was a small nodule on the anterior surface of the liver one-half cm. in diameter. There was an annular, indurated mass about two cm. in length and almost surrounding the jejunum causing slight angulation. There was a hard nodule two cm. in diameter in the mesentery just internal to the main growth. Two nodules in the mesentery of the ileum were removed for section.

There were several nodules from one-half to one cm. in diameter along the left side of the sigmoid and descending colon. Stomach, spleen, and kidneys were normal. Pancreas was enlarged but not hard. There were large, hard, pelvic masses and

Fig. 1.—Gross appearance of bilateral ovarian tumors removed at operation. Note the symmetrical enlargement of the ovaries which maintain their characteristic outline although practically entirely replaced by neoplastic tissue.

Fig. 2.—Segment of jejunum containing the presumably primary neoplasm. This specimen was obtained at the time of the operation for intestinal obstruction. There were large palpable metastases in the mesenteric glands and in the omentum.

the posterior culdesac contained many fine nodules from one-half to one cm. in diameter. Both tubes and both ovaries were removed after separating very dense adhesions. Lateral anastomosis and removal of the growth in the jejunum was

postponed because the condition of the patient was not good. Removal of ovarian growths was done to relieve severe pain in the lower left quadrant, and not because of any hope of cure.

The patient's postoperative recovery was good. Gastrointestinal x-ray series of July 5, 1929 showed the stomach low in position, pylorus spastic, duodenum normal. At six hours, the barium was in the jejunum and ileum, and there was some retention in the stomach. Twenty-four hours showed the barium in the small intestine with slight irregularity in the region of retention high in the abdomen. Examination

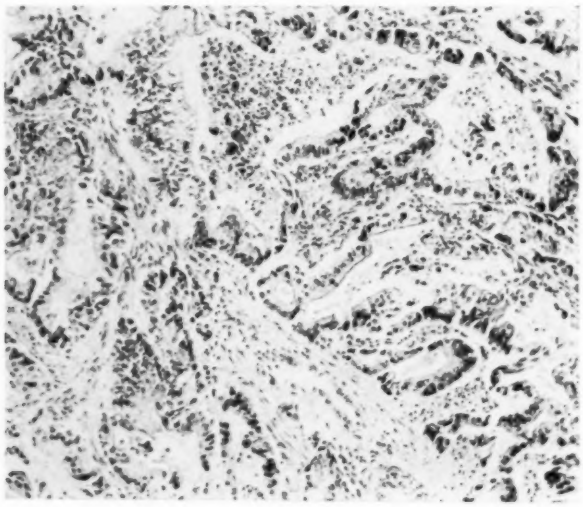

Fig. 3.—This is a section through the lesion of the jejunum. It is quite obviously an adenocarcinoma of the highest grade of malignancy.

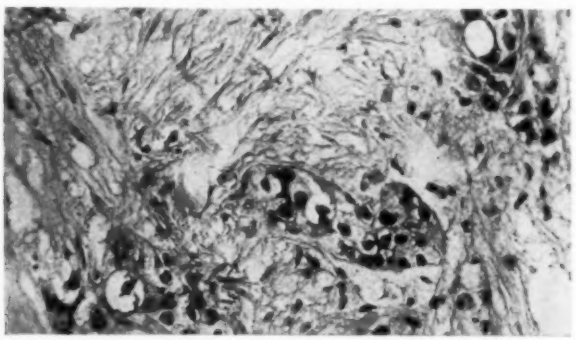

Fig. 4.—This section is taken from one of the ovaries and is identical in structure with other sections taken from various portions of these tumors. There is a typical connective tissue stroma in which are scattered the large mucoid cells characteristic of this tumor. Several typical "signet ring" cells are shown.

showed a fairly marked spasm in the lower portion of the stomach but no organic lesion in the stomach or duodenum. There was some barium retention remaining in the jejunum. On July 12, 1929 a secondary operation was performed to relieve partial obstruction. A left paramedial incision, extending from 2 inches below to 4 inches above the umbilicus was made. The annular carcinoma of the jejunum was excised. The free ends were invaginated and a lateral entero-anastomosis was performed. Abdominal examination was otherwise as before except the sig-

moidal mesentery was enlarged and adherent and contained a nodule the size of a walnut. The condition of the patient improved rapidly after operation, and she was discharged on Aug. 5, 1929 in fair general condition, barring some abdominal pain at irregular intervals. X-rays taken prior to discharge showed no bony metastases.

On Oct. 21, 1929 she was readmitted to the hospital complaining of severe pain in the abdomen, distention, vomiting, and a complete obstruction of the bowel. Examination showed a greatly emaciated white woman weighing about eighty-five pounds. The abdomen was considerably distended and tense. There was occasional peristalic wave visible across the abdomen during which time the pain was accentuated. There was a tender, small nodule below the umbilicus in the midline in the abdominal wall which was slightly movable. There were a few hard inguinal glands. The extremities were markedly emaciated. The patient continued to have a great deal of pain somewhat relieved by morphia until she died on Nov. 12, 1929. The temperature remained normal throughout. X-ray plate of the spine, chest and femur on Oct. 21, 1929 showed a small rounded area at the level of the ninth rib dorsally, four inches from the midline, which might represent metastatic growth. Otherwise x-rays were negative.

Pathologic report: Carcinomatosis. Annular carcinoma of the jejunum with bilateral ovarian metastases. Metastases to the ileum, ureter, liver, peritoneum, mesenteric lymph nodes and wall of the bowel. Microscopic sections of many of the metastases showed well differentiated alveoli. The cells were distinctly outlined and varied between cuboidal and columnar in type, and the nuclei were small and hyperchromatic. Mitosis occur with a moderate degree of frequency. The stroma is abundant, is dense but often loose and cellular toward the edges. The lateral anastomosis was in good condition. The entire pelvis was full of peritoneal metastases which surrounded the gut.

DISCUSSION

This case is unusual in that primary carcinoma of the jejunum with typical Krukenberg secondary growths in the ovaries is very rare, although Roblee, in a recent article, described a case which had its primary adenocarcinoma in the jejunum with secondary growths in the ovaries. The "signet ring" cells and predominances of stroma in the ovarian tumors is very striking in this case. Several cases have been found where the primary tumor is in the sigmoid and cecum, one probably of the bone, but well over 90 per cent are primary in the stomach. Major reports two authentic apparently primary Krukenberg tumors of the ovaries. There are, as pointed out by Major in 1918, three possible ways of the dissemination of the tumor: (1) Retrograde metastases from the stomach and intestines through the lymphatics along the aorta and iliac vessels and by blockage of the lymph glands to the ovaries. (2) Peritoneal dissemination, it being well known that particles of coloring matter placed in the peritoneal cavity are picked up by the ovaries. (3) Blood stream metastases. Major reported a case of metastases into pulmonary blood vessels and into the lungs. In this case, metastases might have been from all three methods: the metastases in the mesentery of the jejunum, ileum, descending colon and sigmoid and a few retroperitoneal lymph nodes suggested dissemination through the lymph glands of the aorta as did

also the fact that the tumor in the ovary was growing apparently from within outward, the serosa being entirely free of tumor growth. These all suggest lymphatic dissemination. However, the presence of many nodules of tumor tissue in the culdesac suggest peritoneal dissemination, this being somewhat offset by the presence of similar nodules in the rectovaginal wall and also by their absence over the rest of the peritoneal surface. Metastatic growths in the omentum and the liver suggest dissemination by the blood stream although autopsy gave no further evidence in support of this.

Miller furnished strong evidence of lymphatic dissemination showing epithelial plugs in the lymph spaces and found, in the different sections, that one could have all stages from the alveolar formation to the breaking-up of these alveoli into irregular clusters of epithelial cells, these again being split into groups of two and three, and finally large signet cells appeared in the connective tissue. Marked variation in microscopic morphology occurs. Ewing suggests for these tumors an origin in the transformation of epithelial cells into spindle cells, as a source for the carcinosarcomatous structures. This, while explaining possibly those cases of authentic primary growths in the ovaries, can have no bearing upon this case.

Jarcho reports, in his cases, that after the tumor had once invaded the tubes and uterus, the posterior bladder wall was always infiltrated, advising against hysterectomy for this reason. Our case may not have reached this stage or perhaps the direction of metastases was not toward these organs for although the fimbria of the right tube showed a few nodules a few mm. in diameter, the rest of the tubes, uterus and bladder wall were free from tumor growth. The rather marked secondary anemia of the patient seemed to be due to inanition and gradual obstruction. The occurrence of almost complete postoperative intestinal obstruction by pressure on the bowel with the anastomosis in good condition from without, together with the occlusion of the left ureter in a mass of tumor tissue involving the rectum, ileum, uterus, ureter with the attendant hydronephrosis was striking.

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TWIN PAPYRACEOUS FETUSES IN TRIPLET PREGNANCY, WITH REPORT OF A CASE

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THE production in utero of a mummified fetus is a well recognized but rare occurrence in association with missed abortion or multiple pregnancy. Mummification and flattening are found almost exclusively in the latter when one fetus dies at an early period and the other goes on to further development. Well characterized papyraceous fetuses are for the most part twins of normally developed, living infants.

The relative infrequency of triplet as compared with twin pregnancy would in itself diminish the incidence of fetal mummification in the former. The occurrence of twin papyraceous fetuses in triplet pregnancy is but briefly touched upon in some of the German books of reference[1, 2] on obstetrics. A search of the available literature has disclosed only twenty mentioned instances. Because of the rarity of the condition and certain points of interest connected with it, a case recently encountered is reported here briefly, and the literature is reviewed to date.

LITERATURE

In a primipara in whom labor occurred at the seventh month, Pretty[3] discovered "some semisolid, movable substances covered with thin membrane," which on being removed proved to be mummified fetuses weighing 4 ounces and 7 ounces. The third child, weighing 3½ pounds, was born alive shortly thereafter. All three were males. There were two placentas, a single and a double one. This case was described before the Royal Medical and Surgical Society of London, and in the discussion a Mr. Ritter stated that Dr. Robert Lee had exhibited a similar one to him five years previously. Two fetuses were of four months' development, and the third alive at full term. He mentioned that Paul Portal had figured a similar case 160 years before.

Van Oteghem,[4] after attending a primipara at the normal delivery of a full-term male, removed the placenta from the vagina by slight traction, and found a portion of the membranes unusually adherent. While he waited, a uterine contraction expelled a formless mass which adhered by a few fibers to the membranes which had remained behind. It was a degenerated placenta, and with it were two flattened fetuses of between three and four months' development.

Lyle[5] reports very briefly the birth of a living eight months child, which was preceded by the expulsion of a blighted fetus that had died at the fourth month. In connection with the placenta there was another blighted fetus apparently of the same age as the first.

Reuss[6] had a case in which, after a full-term living child, two papyraceous fetuses nine centimeters long were born with the placenta.

At the seventh month in a primipara, Small[7] found projecting from the fully dilated cervix a loose body which was easily withdrawn and which proved to be a

papyraceous fetus of four months' development. The birth of a seven months' lifeless fetus with its placenta shortly followed. Then came a second papyraceous fetus with a placenta to which the first one had also apparently been attached.

On the edge of the placenta which was expelled following the breech extraction of a full-term living child from a primipara, Gutman[8] found a gray mass made up of two papyraceous fetuses of four months' development and their degenerated placenta. They had a common chorion but separate amnions, and were single ovum twins. One umbilical cord had a marginal insertion, the other, a velamentous. The course of pregnancy had been normal.

Bazzanella[9] found a mummified fetus of three months development among the blood clots that were expelled with the placenta following the forceps delivery of a full-term living male in a primipara with hydramnios. The uterus contracted and retracted to the usual size, and there was no postpartum hemorrhage. Forty-eight hours later an atrophic placenta with a papyraceous fetus of the same size as the first was expelled.

Sänger[10] observed a delivery at the seventh month of one living and two papyraceous fetuses.

In the instance described by Lambinon,[11] a primipara gave birth normally to a full-term child. In the third stage the midwife found it necessary to interfere because of postpartum hemorrhage, and, after removing the normal placenta, she found that a second remained behind. This was strongly adherent, of a gray color, and of firm consistency, and with it she removed single ovum twin papyraceous fetuses of about three months' development. The cord of the living child had a velamentous insertion.

A midwife brought to Müller[12] some skull bones of a three to four months' fetus which had been expelled as part of an extremely offensive vaginal discharge. His examination of the patient showed an eight to nine months' pregnancy with the uterus irregularly enlarged. The region of the right cornu was higher than the left, and contained the breech. The left cornu was protuberant and hard. The cervix admitted two fingers, and contained membranes and bones. Half the skeleton of a three to four months' fetus having a very bad odor was extracted, and after two days labor occurred normally. The placenta showed in the hard, globular portion which had been palpable externally a second papyraceous fetus enclosed in membranes.

Aldridge[13] found presenting at the vulva in a primipara the foot and leg of a mummified male fetus. After its delivery, the presenting membranes were ruptured artificially, and a living eight and one-half months' female child was born. A second mummified male fetus of four months' development was then expelled. Some difficulty was experienced in removing the placentas. To one of these the two male fetuses were attached while the other belonged to the living female. Aldridge regarded the mummified fetuses as single ovum twins.

The sequence of events was almost identical in the case reported by Nolte.[14] One papyraceous fetus preceded and one followed the spontaneous delivery of a full-term infant in a primipara. They were single ovum twins that had died during the seventeenth week.

At a meeting of the Obstetrical Society of Hamburg, Rueder[15] showed a photograph of triplets, two of which were papyraceous fetuses and the third a premature child. The last was the second to be born, and lived only three hours.

After complete cervical dilatation in a para iv, Moss[16] found a hard mass with spicules on its surface presenting in front of the vertex. On bringing the head to the perineum with forceps, the mass was found to be a papyraceous fetus fitting over it like a bonnet. Following the normal male child there came its placenta and membranes, followed again by a second papyraceous fetus with an atrophied, bilobed placenta having two amniotic sacs and one chorion.

In a para v with mild pregnancy toxemia and hydramnios, Wallin[17] palpated a flattened mass to the right and in advance of the amniotic sac and fetal head. When the cervix had become 2½ inches dilated, this mass was recognized as the head of a papyraceous fetus. It was immediately extracted, and a living child weighing 6½ pounds was later delivered with forceps. Due to postpartum hemorrhage the placentas were removed manually, first that of the living child and then that of the mummified fetus. With the latter there was a second papyraceous fetus in an unruptured sac.

Before the Breslau Gynecological Society Lamy[18] reported finding two papyraceous fetuses in a membranous sac on the placenta which was expelled following the spontaneous delivery of a healthy child in a primipara. They were 8.5 and 7 cm. long, and were flattened to a thickness of 0.8 cm.

On the placenta which followed the spontaneous delivery of a full-term living female in a primipara, Wolff[19] found single ovum twin papyraceous fetuses of about four months' development.

Klimek's[20] patient was a primipara who had a normal labor at full term. Adjoining the normal placenta was a pale, degenerated one with single ovum twin papyraceous fetuses that had died at the fifth month.

In the literature there were found other cases which are so closely related to the subject under discussion that they may be mentioned for the sake of completeness. Both Bertog[21] and Maryanchik[22] describe triplet pregnancies with single papyraceous fetuses. Von Erlach[23] and Sänger[10] mention similar cases. Bretschneider[24] observed a papyraceous fetus accompanying a premature infant and an acardiacus. Two examples of the birth of triplets, one living and the other two macerated, have been recorded, one by Perdu,[25] the other by ten Doesschate.[26] Tartakoff[27] recently observed papyraceous twins in quadruple pregnancy.

REPORT OF AUTHOR'S CASE

H. H., forty-two years old, at full term of her eighth pregnancy, came to the hospital on Sept. 9, 1929 because of a slight discharge of blood from the vagina. Except for an attack of influenza in 1919, which resulted in a stillbirth at the eighth month, she had always been in good health. Her other pregnancies and labors had been uneventful. She had two sisters who were twins, probably double ovum.

Her last menstrual period had begun Dec. 3, 1928, and she had not had prenatal care. During the first two months of gestation she had experienced slight nausea, and in March had begun having bearing down pains in the lower abdomen. They had continued through the remainder of pregnancy, and occurred only when she was on her feet, interfering considerably with locomotion and making her fear that labor was imminent. There had been no bleeding previous to the day of admission, and the abdomen had enlarged steadily as in previous pregnancies.

The patient was of medium build and in apparently good health. General physical examination was essentially negative except for the findings of a full-term intrauterine pregnancy with the fetus in R.O.A. presentation and position, the presenting part at the pelvic inlet, and the cervix 3 cm. dilated. Pelvis was normal. Blood pressure 135/90. Blood Kahn reaction and urine were negative.

Labor pains began shortly after admission, and a living female child weighing 3600 gm. was born spontaneously four and one-half hours later. After ten minutes the placenta was easily expressed from the vagina, but seemed to be adherent to the uterine wall at one margin. Gentle, continued traction on the portion already delivered resulted in the removal of a mass of gray tissue which on careful examination proved to be a degenerated placenta with single ovum twin papyraceous

fetuses. Total blood loss during the third stage was estimated at 300 c.c. The puerperium was afebrile, and mother and child were discharged in good condition on the eleventh day.

The appreciation of the true condition presented by the secundines was clear only after their careful inspection. Together they weighed 820 gm. The placenta of the living child was entirely normal. It measured 24 × 15 × 2 cm., and showed a few white infarcts on its fetal surface. The rupture of the membranes was near the placental margin. Insertion of the umbilical cord was eccentric, and its length 40 cm.

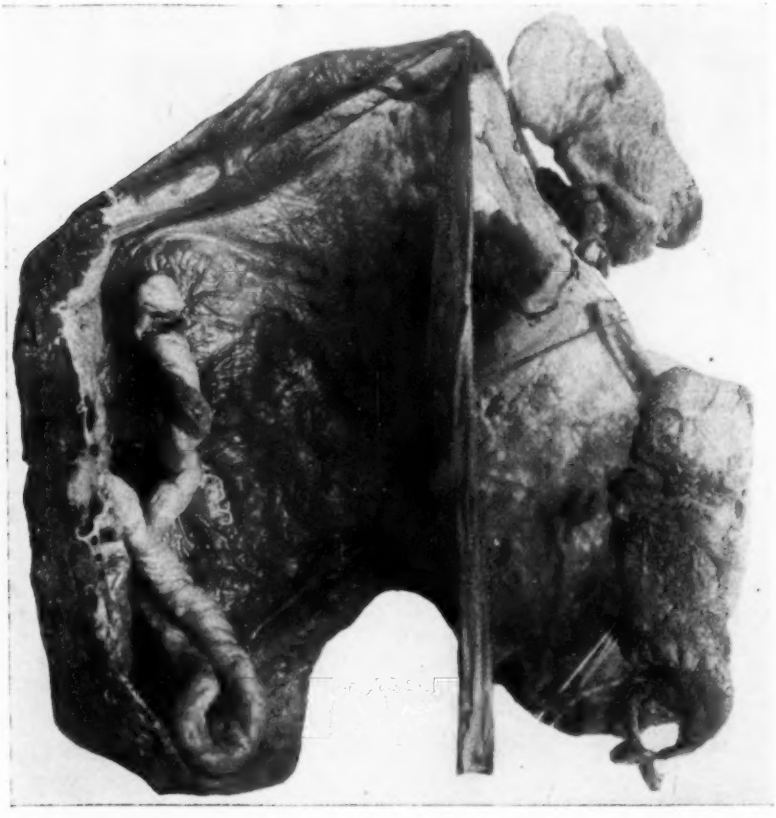

Fig. 1.—Normal and degenerated placentas with twin papyraceous fetuses in association with the latter.

Adjoining this placenta over a distance of 9 cm. and forming a continuation of its long diameter was a second one, pale, yellow, hard, and fibrotic, measuring 15 × 10 × 0.5 cm. The demarcation between the two was sharp and striking. The fetal membranes corresponding to the degenerated placenta were throughout almost their entire extent loosely adherent to those of the living child. On separating the two chorionic sacs it was found that pale, friable, but intact membranes were collapsed on the placental surface and that they contained within them two flat, ovoid bodies measuring about 4 × 10 cm. and only slightly elevated above the general level. The one lay near the center of the placenta, the other near the periphery. After opening the membranes containing them, these bodies were recognized as papyraceous fetuses. Each was enclosed by a definite amniotic sac from which the fluid had been absorbed, and the whole was enveloped by one chorion.

Although they had been firmly pressed against the placental surface, which showed no trace of blood vessels, they had made no depressions in it. The parts of each were so pressed together and the surface inequalities so filled in with a gray material resembling vernix caseosa that their first appearance was that of formless masses of dried, mummified tissue. Closer observation revealed the contour of the ribs through the closely applied skin, and, after extending the extremities, each mass took the form of a dried, flattened fetus of tanned appearance, with gray, wrinkled skin lying close to the bones and with the skull flattened from side to side. Their sex could not be recognized externally. The intestines of each were exposed and bile stained. The umbilical cords were delicate and fragile, measured 18 and 15 cm. in length, and, as nearly as could be determined, had direct placental insertions. Both fetuses had a crown-heel length of 13 cm. It is evident from the data given that they were single ovum twins that had reached about the fourteenth week of development. Roentgenograms of the fetuses showed a stage of ossification of their skeletons corresponding with the beginning of the fourth lunar month.

DISCUSSION

Of the nineteen cases of triplet pregnancy with twin papyraceous fetuses found described in the available literature, eleven occurred in primiparae and three in multiparae. In five cases the parity was not stated. The third triplet was premature in six instances, and one of these was dead. Seven of the pairs of papyraceous fetuses were single ovum twins. In the remaining cases their relationship was not definitely stated. Their period of development was not given in five cases, and in the remaining fourteen it had been arrested between the third and fifth months. As to the order of birth, one time both preceded, eight times both followed, and eight times one preceded and one followed the normally developed child. The order was not mentioned twice.

Concerning the cause of death of one or more fetuses early in the course of multiple pregnancy little is known. Lamy[18] regarded a fall at the third month as the probable etiologic factor, and Small[7] attributed it to the impoverished general condition of his patient. The woman observed by Müller[12] had bumped her abdomen against the corner of a stove between the third and fourth months. No one else even hazarded an opinion as to what may have been responsible in his case. From the information at hand about the one here reported no conclusion can be drawn. Among the causes that have been advanced there may be mentioned localized abnormalities of the decidua interfering with placentation, mechanical insults, lesions of the cord, and developmental anomalies incompatible with life. Inequality of circulation resulting from anastomosis of vessels in a common placenta or from the third circulation could not account for the death of both fetuses derived from one ovum.

In none of the cases reviewed were any symptoms mentioned which might have indicated with any great probability the early death and retention in the uterus of one or more fetuses. Toxemia of pregnancy

and hydramnios occurred a few times. In Small's[7] case the uterus was irritable for a month preceding delivery, and in that described by Pretty[3] there had been abdominal tenderness from the start. In the latter placenta previa was a complicating factor. Klimek's[20] patient suffered with severe backache for a few days during the fifth month of pregnancy. According to Strassmann[1] transitory bleeding may occur as the result of the death of one ovum. Wolff[19] observed this symptom in his case, but, as he states, it is too frequent from other causes to be of any diagnostic significance.

Halban[28] followed a case of twin pregnancy in which the death of one fetus in the fifth month was marked by the sudden diminution of acutely developed hydramnios, the onset of painful uterine contractions which persisted until the end of pregnancy, and the development of a furrow across the uterus which apparently indicated the boundary between the normal and dead ovum. He believed that such findings would be of definite value in diagnosis. It is interesting to note that in the case here reported intermittent pains appeared around the time of the death of the one ovum, and that the uterus was unusually irritable throughout the remainder of gestation. The foreign body action of the dead ovum was in all probability responsible for this. The patient was questioned regarding a sudden diminution in size of her abdomen or a temporary cessation of its enlargement, but had noticed neither. No furrow of the kind described by Halban was present. It is apparent that a diagnosis depending upon such criteria can rarely be made, and that the condition will have to be recognized by close observation at the time of delivery. It seems doubtful that the osseous system of a small papyraceous fetus would be dense enough to make possible its visualization with the x-rays.

The clinical importance of single or twin papyraceous fetuses is not great. When presenting first they may give rise to obstruction of labor or, more frequently, to diagnostic errors. Their retention may result in postpartum or puerperal hemorrhage or puerperal infection. Small papyaceous fetuses are recognized only by careful examination of the after-birth. They are probably often overlooked, and their occurrence is doubtless more frequent than the small number recorded in the literature indicates. Bazzanella[9] discovered a papyraceous fetus among the blood clots that came with a normal placenta. He concluded logically that at least a degenerated placenta must have been left behind, but did not interfere because there was no abnormal bleeding. After forty-eight hours the second placenta with a second mummified fetus was expelled.

SUMMARY

1. The occurrence of twin papyraceous fetuses in triplet pregnancy is rare. A case is here reported, and data are brought together on nineteen out of twenty others found in the available literature.

2. A papyraceous fetus is found almost exclusively in multiple pregnancy which advances to or near term. Mummification is most frequent in fetuses dying between the third and sixth months of development.

3. Regarding the cause of early death of one or more fetuses and continued development of one or more others there is no information that is convincing.

4. There are rarely any symptoms or signs that suggest such an occurrence, and the diagnosis can be made definitely only at the time of delivery. Even then it may be missed by careless examination of the secundines.

5. A papyraceous fetus is of some clinical significance since it may cause diagnostic errors, exceptionally obstruct labor, or, through its retention, result in postpartum or puerperal hemorrhage or puerperal infection.

I wish to thank Dr. Ward F. Seeley for permission to report this case and Dr. Joseph A. Kasper for preparation of the specimen for photography.

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216 South State Street.

ANILINE POISONING IN THE NEWBORN, WITH A REPORT OF THIRTEEN CASES*

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THIS paper will describe thirteen cases of an unusual type of poisoning that occurred at the Kings County Hospital on October 28, 1929, in the service of Dr. H. M. Mills.

Hospitalization *en masse* is a necessary means of handling the sick of a community. It has numerous factors in its favor, but also has many factors that we accept only because we must, and not because we so desire. It is only necessary to cite one or two to impress upon our minds how undesirable hospitalization can be at times; such as the rapid spread of impetigo on a children's ward, or any form of contagious disease, as measles, diphtheria, etc. The above are what one would call the usual dangers of hospitalization. This paper will deal with an uncommon and really unsuspected source of danger, one that could excusably be overlooked.

The obstetric ward of the Kings County Hospital generally has a census of 30 to 50 newborn infants. These patients are handled in a routine manner, each baby receiving every care that all the others receive and also at the same times of the day. Similarly, all of their clothes come from a common laundry, and the babies receive complete changes of attire at the same times. Therefore, if the clothes were to act as a common carrier for a danger to the welfare of these patients, they would all be exposed to it in essentially the same manner and to the same degree.

On Saturday, October 26, 1929 (two days before the onset of the present trouble), Ward 18—the obstetric service—received a new supply of babies' apparel and blankets. These were all freshly stamped in large type with the identifying lettering WARD 18, K.C.H. This is the laundry mark so that in the future when returning from the laundry, the articles will reach their proper destination. These articles of clothing were put in use about 7 o'clock Monday morning, so that by noon practically every child had some fresh articles of clothing in contact with its body.

At 4 P.M. of that day, the nurse in charge of the babies called the intern's attention to baby K, who apparently had taken a sudden bad turn. On examination, the baby was observed to have a marked cyanosis of its skin, particularly of its lips, mucous membranes, eyelids, forehead, ears, and extremities. Respirations and pulse were rapid, but the temperature was normal. The child had refused its

*Read at a meeting of the Brooklyn Gynecological Society, April 30, 1930.

3 P.M. feeding, and at that time appeared drowsy, weak, and apathetic; and was entirely unresponsive to handling. Its general appearance was that of a bluish colored wax doll. Complete physical examination revealed nothing wrong except the marked cyanosis, cold extremities, and rapid respirations and heart action. Expectant treatment was instituted.

It was further noticed that the babies as a group were reluctant about taking their 3 P.M. feeding. At about 5 P.M. baby K had a particularly bad spell, during which he seemed to be gasping for air. This lasted a few minutes and the baby then returned to its previously cyanosed and lethargic condition. Between 4 and 5 P.M. three other babies were observed to be cyanosed; namely, babies Kl, B, and C.

At about 5 P.M. baby B was observed to be quite stiff in addition to his marked degree of cyanosis. This stiffness lasted for a few minutes and then subsided, and the baby was then in quite a similar condition to baby K. At the 6 P.M. feeding the babies as a group were more reluctant about nursing than previously, and some refused to nurse at all, acting as though they were asleep at the breast. When the infants were being returned to their cribs, the nurses observed that many more babies were cyanosed and drowsy. This of course excited some alarm. Due to the general involvement, it was assumed that there must be a common agent to explain the sudden illness of thirteen babies out of a total of thirty-two. The first thing considered was possible carbon monoxide poisoning. However, the only source for this poisonous gas could be the illuminating gas supply, and no leakage was discovered. For that matter, the atmosphere of the room appeared to be quite normal, as the nurses had been in the room as long as the babies without the slightest maleffects. Despite our self-assurance that the atmosphere was not unduly contaminated with unhealthy amounts of carbon monoxide gas, the room was thoroughly ventilated. No definite improvement in the condition of the cyanosed infants was observed. Finally it was found that the linen had been put into use without first being boiled and washed. The new linens were investigated and found to have fresh print on them, as has been previously described. In practically all the cases, the printing was found to be in contact with some part of the babies' bodies; in fact, definite staining was found on the skin of eight of the thirteen babies. We now felt certain that the etiology of this unusual poisoning was discovered.

The immediate measures that were undertaken to eradicate the danger were as follows:

1. All new linens were removed from contact with the infants.
2. The babies were thoroughly washed with alcohol or ether to remove all of the print stains, and were then clothed in linen that had already been boiled and washed.

3. Administration of a mixture of oxygen and 5 per cent carbonic acid to babies as needed.

4. Careful observation of all babies every few minutes, so that immediate measures could be undertaken if a patient suddenly became worse.

In order not to overburden the nursing staff and the laboratory technician, three cases were chosen at random for a complete work-up. We felt that the findings in the three cases would be typical of the group. Therefore, in these cases a study was made of the temperature, pulse, and respiration, and blood specimens were examined by means of a spectroscope to discover whether or not methemoglobin was present. In two of the three cases blood counts and uranalysis were done. However, in all cases a detailed study was made of the symptomatology and clinical findings that were presented; and we therefore studied the cases as to the degree of cyanosis; where the cyanosis was most evident; how the babies nursed; the degree of apathy; the type of response to stimuli, such as handling the baby; whether convulsions were observed; as to the definite finding of dye stains on the babies' bodies; the type of cry, whether strong or weak; the condition of the extremities; and lastly the subsequent course of the cases.

The spectroscopic examination of the blood in all three cases showed the definite presence of methemoglobin.

The urine examinations revealed only slight changes from the normal; that of baby K had a light amber color, cloudy appearance, a very faint trace of albumin, no sugar, gave an acid reaction, and contained a few leucocytes, many uric acid crystals, a few epithelial cells, an occasional red blood cell, and amorphous urate sediment. That of baby B had a light amber color, appeared cloudy, gave an acid reaction, contained no sugar or albumin, and had a few epithelial cells and a few leucocytes.

The blood counts showed no unusual findings but that of suppression of the total leucocyte count in both cases, and a definitely low red blood cell count in one case. However, the baby with the low red blood cell count normally was quite pale and sallow complexioned. The blood pictures were as follows:

Baby K		*Baby B*	
W.B.C.,	10,600	W.B.C.,	7,200
Polymorphonuclears,	47 per cent	Polymorphonuclears,	53 per cent
Lymphocytes,	37 per cent	Lymphocytes,	34 per cent
Large monocytes,	13 per cent	Large monocytes,	12 per cent
Eosinophiles	3 per cent	Eosinophiles,	1 per cent
R.B.C.,	3,500,000	R.B.C.,	5,590,000

In summation of our detailed study of the clinical findings, we observe:

1. The pulse in every case became very rapid but maintained its regularity and rhythm.

2. There was no variation of the temperature from normal.

3. Respirations were greatly accelerated but continued regular.

4. Cyanosis was marked in practically all cases.

5. Cyanosis was most evident on the lips and eyelids.

6. All suffered from anorexia.

7. The degree of apathy was pronounced in practically all cases.

8. The response to stimuli was decreased in every instance.

9. Only one case showed what we could consider a convulsive seizure.

10. Dye stains were found on the skin of eight of the thirteen babies.

11. The cry was decreased in strength in every case.

12. The extremities tended to be cold and cyanosed in all cases.

13. The subsequent course showed complete recovery in every case within a period of from twenty-four to seventy-two hours, without any observable harmful effects.

The dye was analyzed by Dr. G., pathologic chemist of the City of New York, who stated that the dye mixture contained phenol (carbolic acid), levulinic acid, aniline, and induline dye (spirit soluble). He added that the cyanosis could result if either the phenol or aniline was absorbed. However, Dr. G. did not believe the dye itself could have caused this condition, as "it would not be absorbed; first, because the molecule is very large, and second, because the dye is extremely insoluble in water."

In refutation, we may mention the work of Rayner[1] who, as far back as 1886, exposed the skin of a normal healthy child to aniline and observed that the infant developed symptoms exactly similar to those of the cases of suspected aniline poisoning that he had under his observation. Unquestionably many similar cases have occurred in the past, and we will be forced to accept the fact that one of the above substances, probably aniline, was the cause of our cases of poisoning.

A review of the literature covering this unusual type of poisoning reveals the fact that aniline poisoning is closely allied to nitrobenzene poisoning as to mode of susceptibility, symptomatology, and the effects manifested. For this reason writers have tended to report the cases as "dye poisoning"; and whether or not the specific poisoning substance was aniline or nitrobenzene was of little moment, as they produced similar types of reactions in the living organism. Conflicting statements are found in the literature as to the toxicity of aniline and nitrobenzene. Miner[7] believes that the true toxic agent must be a by-product associated with the chemical substance, as otherwise he presupposes the occurrence of many more cases than have been reported. In refutation to the above statement, we may quote Muehlberger[10] who states that probably many times more cases of dye poisoning actually occur than are reported. He also adds that, "It is now

definitely known that nitrobenzene and aniline, when pure, are toxic and absorbed through the skin."

All of the accepted authorities are not entirely in accord as to the way in which aniline causes its poisoning phenomena. Young believes aniline poisoning causes a cardiac type of death. In his studies he at no time found evidence of methemoglobin in the blood of his subjects, but by means of electrocardiographic studies he observed that the specialized conducting tissues of the heart were affected and produced heart-block. This worker further observed that the heart stopped beating before the cessation of respiration. The blood in these cases was observed to be of a brownish color and just before death showed an increase in the red blood cells, hemoglobin, and oxygen capacity of the blood. On the other hand Zeligs[9] and Neuhoff,[3] in independent articles, state that the symptomatology is the result of the formation of methemoglobin in the blood. By this means the oxygen content is reduced from a normal of 17 per cent to as low as 1 per cent. The tissues are therefore poorly supplied with oxygen and symptoms of asphyxia supervene. In view of our observation of three blood specimens containing methemoglobin by spectroscopic test, we are inclined to concur with Neuhoff and Zeligs, as to methemoglobin being the chief factor in causing the poisoning symptoms. In further support of this opinion we may cite Cushing[2] who states that the poisoning action of aniline results from the formation of methemoglobin in the blood. Young in his studies showed that when 0.1 of a gram of aniline per kilogram of body weight was injected into the vein of a dog, death resulted in a few minutes, death being cardiac in type.

Treatment of aniline poisoning is a relatively simple procedure. It consists of removal of the dye-containing clothing from the patient. The skin should then be thoroughly cleansed with alcohol or ether in order to remove the dye that may be adherent. Where dyspnea and cyanosis are most marked, the inhalation of a mixture of oxygen and 5 per cent carbon dioxide is of value. Stimulants, such as camphor and oil, caffeine, sodium caffeine benzoate, and adrenaline are used as indicated. Fluids should be pushed continuously. However, the most important consideration is prophylaxis; all danger from this source of poisoning can be eliminated by simply boiling all freshly stamped linens, as in this way the dye is inactivated.

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1650 FORTY-NINTH STREET.

A CASE OF NOSENCEPHALUS WITH EVENTRATION OF THE ABDOMINAL AND CHEST ORGANS, POLYHYDRAMNIOS, AND OTHER ANOMALIES

By Silik H. Polayes, M.D., and Jacques D. Soifer, M.D.,
Brooklyn, N. Y.

(From the Department of Pathology of the Jewish Hospital)

MRS. L. K., a gravida i, aged twenty-seven, was admitted to the private obstetric service of Dr. H. B. Boley on June 6, 1929. The family history was irrelevant. Appendectomy six years ago. Patient was married three years and has had several "stretchings" for sterility. The menstrual history was normal. The last regular period occurred November 2, 1928, but the patient could not recall whether a dilatation had been done after the last menses. Upon examination she was found to be pregnant and measurement of the pelvis showed a deep symphysis, slight narrowing of the pubic arch and a prominent left ischial spine.

The pregnancy progressed normally for the first thirty weeks, then the abdomen began to enlarge very rapidly—and toward the end of the thirty-first week, the size of the uterus was larger than that of a full-term gravidity. A monstrosity was suspected at this time. A week later, on June 6, 1929, about 4 P.M., while the patient was at home, the membranes ruptured spontaneously and large quantities of amniotic fluid escaped. The exact amount could not be estimated. One hour later, the patient was admitted to the hospital, although she was not in labor.

Abdominal examination showed the height of the fundus to be that of a thirty-two weeks' gravidity. The breech was in the fundus, the small parts were to the right, the back was toward the left, and the fetal heart sounds were best heard in the left lower quadrant. Per rectum, the cervical canal was found effaced, the cervix thinned out, and the external os showed one finger dilatation. The presenting part was approximately at the level of the ischial spines. Fluid was escaping from the vagina. Temperature and pulse rate normal. Blood pressure was 120/78.

At eight o'clock the next morning (labor began at 3 P.M.), the external os was fully dilated. Vaginal examination revealed a compound presentation, consisting of the left shoulder (Sc.L.A.) and the right hand. A version and breech extraction were done with the delivery of a stillborn monster. The placenta, normally situated, was expressed ten minutes later. It showed no gross pathology. There was no undue postpartum bleeding. The puerperium was uneventful except for a rise in temperature to 100.8° F. on the second day. The patient was discharged on the twelfth day.

The Wassermann and Kahn tests of the patient and her husband were negative. The microscopic examination of the placenta showed no evidence of syphilis. There were no abnormalities in the patient's genital tract; but an hydramnios was present, a frequent association with monstrosities.

Description of Monster.—The fetus, a male, 32 cm. in length, presents three different major anomalies; cranioschisis, thoraco- and hypogastroschisis, and eventration of all the viscera. There are many lesser abnormalities.

The cranioschisis is of the anteromedian type (mero-acrania); both the parietal and frontal bones are almost entirely lacking. The brain is represented by a small

portion of cerebrum which is scarcely recognizable as such, being a conglomeration of brain tissue and blood. The cerebellar tissue is more easily distinguished, but is vestigial and cystic in character. The whole mass, covered by a thin membrane, apparently meninges, is exposed, due to the lack of cranial bones and integument (nosencephalus).

The cranial bone deformity and a marked exophthalmus give the face a frog-like expression. The forehead is markedly narrowed, due to the frontal bone defect. There is almost a complete absence of nasal bones, producing a flattening of the bridge of the nose and an undue prominence of the alae nasi. A cyst about 1 cm. in diameter, is attached to the right ala. There is a marked harelip and cleft-

Fig. 1.—Anteroposterior view.

palate. The undeveloped inferior maxilla produces a receding chin. The aural appendages are rudimentary and the neck is reduced to a mere fold of skin, due to the defective cervical vertebrae.

The sternum is absent, which causes a defect in the anterior chest wall. The entire thoracic cavity is exposed and its contents are almost completely eventrated. The anterior abdominal wall is wholly lacking and the celomic organs are likewise eviscerated. The chest and abdominal cavities are greatly distorted by the extreme lordosis and scoliosis of the spinal column. The photograph (Fig. 1) depicts rather vividly, the anomalous relations of the thoracic and abdominal viscera. The liver is very large and conceals the chest organs. The lungs are compressed by the dome of the liver and the curvature of the thoracic vertebrae. The heart and pericardium are displaced to the left, and its apex can be seen exposed between the liver and the ribs that form the margin of the open chest cavity.

The loops of intestine which protrude in a chaotic mass, are entirely outside of the body. The kidneys and related internal genitourinary organs, although hidden by intestines, are also eviscerated. The pubic bones have failed to unite producing an extrophy of the bladder. The external genitalia are markedly enlarged. Both testes have descended into the scrotum which is thick-walled. The corpora spongiosa and the glans penis are considerably hypertrophied.

The left upper extremity is represented by a small prominence of skin and subcutaneous structures adjoining the acromial end of the clavicle. To a point just below this projection is attached a cord-like mass consisting of skin and subcutaneous tissue, which is attached at its distal end to the back of the trunk.

Fig. 2.—X-ray picture of fetus in position shown in Fig. 1.

The right upper extremity shows a compensatory hypertrophy. It is rigidly twisted around the back of the fetus so that the thumb points to the left buttock. The fingers are tightly flexed and webbed. The joints of the lower extremities are all acutely flexed. The right foot is hooked around the left leg. The toes are webbed. There are no supernumerary digits. The soft tissues of the buttocks and thighs are unduly thickened due to the overdevelopment of the musculature in this region.

COMMENT

This case is reported because it is an extremely unusual type of monster. Greenhill, Pribram and Brochocki have pointed out somewhat similar cases. Ballantyne, describing this anomaly, cites a few cases, and emphasizes its infrequency. A thorough search of the literature for other monstrosities of this character

is difficult. In the first place, there is no standard classification of monsters, but a host of classifications, many of which are quite complicated and inapplicable. Second, monstrosities are frequently incorrectly classified by authors who report these cases. For example, acrania is often confused with acephaly, exencephaly with anencephaly, anencephaly with acrania, et cetera. Third, cases may be hidden in articles, the titles of which give no clue to the subject that is being investigated. Fourthly, the titles of papers are often ambiguous, as, for example, "An Unusual Monstrosity" or "A Rare Fetal Anomaly."

A plea is therefore made for a standard nomenclature which will make possible a satisfactory classification of fetal monstrosities. It is also urged that case reports should be accurately and clearly titled.

REPORT OF TWO CASES OF TWIN PREGNANCY WITH EARLY DEATH OF ONE FETUS*

By T. J. Parks, M.D., Fairfield, Ala.

AT THE Employees' Hospital of the Tennessee Coal, Iron, and Railroad Company approximately 400 patients are delivered a year, almost half of whom make visits to the prenatal clinic. Some of the remainder are sent in by district physicians because of obstetric difficulties; others for various personal reasons.

Out of all the cases that have been delivered at this hospital since it opened its doors in November, 1919, the two cases about to be detailed are the only ones on record here; and, unusual as it is, they came within one week of each other. Such cases are only mentioned as possibilities in textbooks on obstetrics. A survey of the recent American literature does not reveal any similar cases, and the Package Library of the American Medical Association could not furnish me with any literature on the subject.

Neither of the patients was cared for in our prenatal clinic. The first and more striking case came to the hospital because of the spontaneous rupture of the membranes and escape of clear fluid before the onset of labor; the second case was sent in, after being seen but not examined by a district physician, with the diagnosis of placenta previa, because of the bloody fluid that she passed vaginally, without having any labor pains.

Case 1.—Mrs. G. M., white, American, multipara, aged thirty-three, was admitted to the hospital in the last trimester of pregnancy, in early labor. She was in good physical condition. Blood pressure was 100/60, urine negative, no signs of toxemia, Wassermann negative, membranes ruptured, fetal heart sounds normal.

She had always enjoyed good health, except for bronchial asthma the past four years.

Her maternal grandmother was one of twin sisters, who were said to resemble each other closely. Her great aunt on her mother's side was one of twins, and they looked alike. There were no twins on her paternal side. The patient's husband's maternal grandmother was one of twins, and he had an aunt who bore twins. He himself was one of twins, both of whom were boys; but his twin, who was as large as he, was born dead.

The last menstrual period ended thirty-two weeks before admission, but it was abnormal on account of its brevity.

The patient had had four normal full-term babies and no miscarriages.

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*Read before the Jefferson County Medical Society at Birmingham, Alabama, February 17, 1930.

During the present pregnancy she had not felt as well as in former pregnancies. Nausea began about the tenth week, which persisted until after delivery. The week previous to the rupture of the secundines, she was troubled by a profuse, irritating leucorrhea with a foul odor.

Labor proceeded normally, and a well-formed male infant, weighing 1350 gm. and measuring 39 cm. from vertex to external malleolus, was born. The after-birth came ten minutes later.

Upon inspection, the after-birth (Fig. 1) was found to be composed of one piece, half of which appeared normal on its maternal and fetal surfaces; the other half was flattened and grayish on its maternal surface. The membranes of the latter

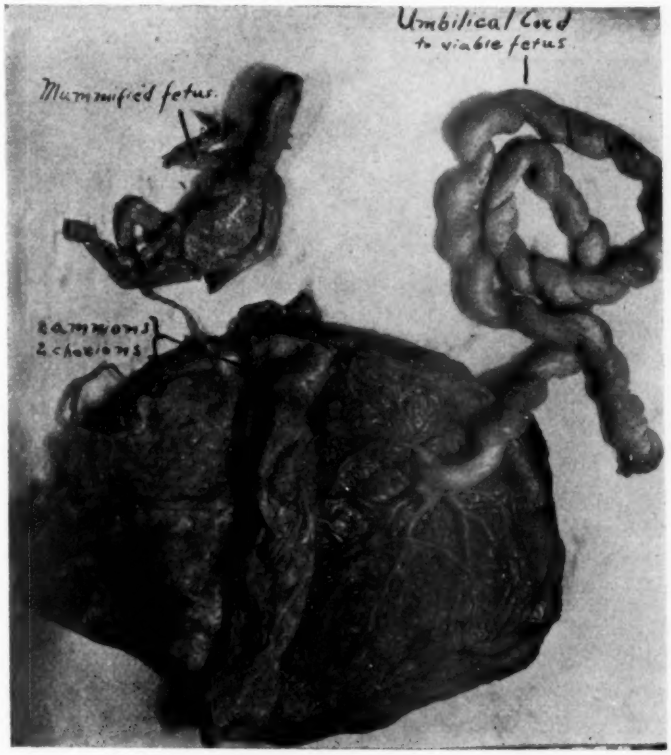

Fig. 1.—Fetal surface of placentas of Case 1 with two amnions and two chorions rolled to center.

half were loose, but intact. Upon opening the sac, a dead fetus 14 cm. long was found in a state of perfect preservation. It was attached to the placenta by an umbilical cord corresponding in size to that of the fetus. The fetus was only slightly compressed, although surrounded by only approximately two or three ounces of clear almost odorless fluid, which was slightly darker than normal amniotic fluid. There were two amnions and two chorions. The placentas were approximated to each other. One appeared normal, microscopically; it measured 16.0 by 11.5 by 2.7 cm. The flattened, hard placenta appeared markedly fibrotic and the villi were decreased in number. It measured 14.0 by 8.0 by 0.8 cm.

CASE 2.—Mrs. R. T., white, American, multipara, aged twenty-seven, was admitted to the hospital with diagnosis of placenta previa. She was in good condition. No

pains, no bleeding, blood pressure was 120/68, fetal heart normal. No evidence of placental tissue was found on vaginal examination.

Family history irrelevant, no twins on either side.

Last menses ceased thirty-six weeks before admission.

She had had two normal full-term babies, and one miscarriage at five months, cause unknown.

During the present pregnancy she had not had any discomfort. Upon careful questioning, it was found that there was a profuse flow of fluid and that it was only blood tinged. She went into labor spontaneously the same afternoon as admitted, and was delivered a few hours afterward of an apparently normal female

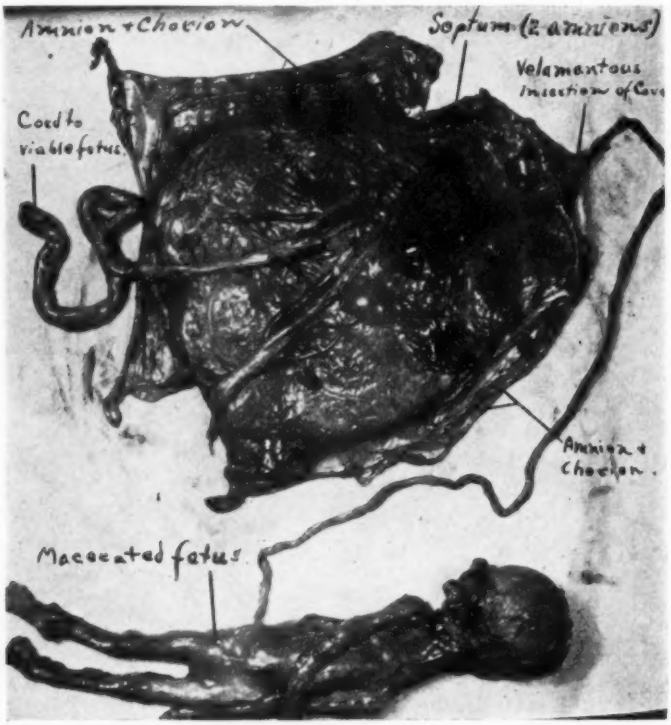

Fig. 2.—Fetal surface of placenta of Case 2 showing septum of two amnions and velamentous insertion of umbilical cord.

infant, weighing 1772 gm. and measuring 43 cm. from vertex to external malleolus. The placenta (Fig. 2) protruded from the vagina immediately following the child. The maternal surface was found to appear normal, except for a small area on one edge that was firmer and had a larger number of grayish streaks than the remainder of the organ. The fetal surface was found to be divided into two unequal portions by two thin membranes. The larger portion was normal in appearance. The smaller division contained a macerated fetus 23.5 cm. long. The umbilical cord was attached to the secundines. There were two amnions and one chorion in this case. Both amniotic sacs had ruptured before birth.

The entire placenta measured 15.5 by 15.5 by 2.3 cm. The microscopic appearance of the placenta was normal, except for the firm area which showed a moderate amount of fibrous tissue.

COMMENT

Both of these cases are probably uniovular in origin; Case 1 because the placentas are approximated, and Case 2 is definitely so, as there is but one chorion.

The cause of the early death in Case 1 is not clear. Some of the causes of early intrauterine death in general are: embolus of a large vessel, torsion of the umbilical cord, developmental anomaly or relative weakness, and the occurrence of a retroplacental hematoma. As the placental area supplying the fetuses in Case 2 was so unequally divided, it must be concluded that asphyxia from developmental anomaly was the cause of the intrauterine death in this case.

Mrs. G. M. probably went into premature labor because of a diseased cervix and the inevitable local infection of the membranes and the resultant weakening which predisposed to their rupture. The same thing could have been true in Case 2. However, it seems more likely that it was nature's method of ridding the uterus of a macerated fetus.

Watson has shown, experimentally, in rabbits[1] that amniotic fluid is not secreted after fetal death, which fact is borne out in Case 1.

The placenta and dead fetus in Case 1 were held in place by the pressure exerted by the intact membranes and adherent placenta of the living twin. It has been shown that a uterus does not attempt to cast off its contents until a zone of separation has been formed.[1]

The placenta of the fetuses in Case 2 has anastomosing blood vessels just as any single placenta. Also, in this case the fetus evidently died first, and, as is the rule in such cases, the placenta kept developing for a considerable length of time afterward.[2]

I am indebted to Dr. Walter C. Jones, Pathologist, Employees' Hospital, Fairfield, Alabama, for the microscopic examination of the placental tissue and for his very helpful advice.

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Bilateral cortical necrosis, resulting from infarction of the cortical or interlobular arteries and occurring postpartum in cases of toxemia of pregnancy, is rare. A typical instance of this condition together with autopsy findings is reported in this paper.

EHRENFEST.

PREGNANCY AS A COMPLICATION OF NEUROFIBROMATOSIS

(von Recklinghausen's Disease)*†

By J. Irving Kushner, M.D., New York, N. Y.

ALTHOUGH reports on the association of neurofibromatosis and pregnancy have so far been very few, it has been the surmise of all those who have studied the subject that the incidence of this condition is probably much greater than the few reported cases would indicate. The impression exists that the condition is frequently unrecognized. Especially has this idea been impressed upon us, when during the past year we have seen four cases, in an obstetric service of only moderate extent.

Tumors of the peripheral nervous system form a very important and complex group of neoplasms of frequent occurrence and varied clinical course. In one general group the growth affects the connective tissue structures of the nerve, the tumors are fibrous in character and are commonly classed as fibromas. When they are multiple we have the condition known as "von Recklinghausen's disease" or neurofibromatosis. The cause is unknown. It is assumed to be a congenital disease, sometimes familial and rarely hereditary. Generally the disease is benign and frequently characterized by no symptoms. If the tumor compresses a nerve severely, objective sensory disturbances may occur.

Cases seen in the Bronx Hospital are here given:

R. M. No. 25503. Age 20, Irish, para i. She was first seen in prenatal clinic on October 8, 1929, being then seven months pregnant (last period April 6, 1929). Her measurements were normal. The fetal heart was heard in the right lower quadrant. The fundus was one finger above the umbilicus. Blood pressure 110/60. Urine negative.

It was noticed that she had multiple pea-sized nodules developing in the subcutaneous tissue, over the entire body and extremities. These tumors were freely movable, hard, and tender; with pigmentation of the overlying skin. A diagnosis of neurofibromatosis was made which was confirmed by the consulting dermatologist, Dr. A. Rostenberg.

The patient stated that she first began to notice the nodules eleven years previously—and that there had been no increase in these lesions for seven years. In February, 1929, she was a patient at the General Memorial Hospital where a diagnosis of neurofibromatosis was made. At that time she received three x-ray treatments.

On January 14, 1930, she was delivered spontaneously of a male child weighing eight pounds and normal in every respect. She made an uneventful convalescence.

F. H. No. 23113. Age 34, Jewish, para iii. She was seen first in the prenatal clinic on November 15, 1929, with small nodules over costochondral junctions and entire back; also numerous brownish, circular pigmented nodules from 1 mm. to

*From the Obstetric Service of Meyer Rosensohn, The Bronx Hospital, N. Y.
†Read before the Clinical Society of The Bronx Hospital on May 12th, 1930.

3 cm. all over skin of the body. A diagnosis of neurofibromatosis was made and confirmed by Dr. A. Rostenberg, the consulting dermatologist.

She was delivered spontaneously of a normal child and was discharged after an uneventful convalescence.

S. S. No. 23624. Age 29, Jewish, para ii. She was seen on January 3, 1929, in the prenatal clinic. She showed irregular areas of brownish pigmentation generally distributed over the trunk of her body, along with some superficial fibromatous nodules about the size of a pea. In addition there were numerous soft, slightly protruding areas of a brownish-red color easily invaginated. A diagnosis of von Recklinghausen's disease was made.

She was admitted to the hospital in active labor on April 10, 1929, and delivered spontaneously of a normal child.

In a dermatologic consultation with Dr. S. Feldman on the third day postpartum the diagnosis was confirmed.

B. F. No. 24076. Age 39, Jewish, para iv. Seen in the prenatal clinic three months before delivery with multiple papillomata and small raised pigmented areas over the chest and back. The diagnosis of neurofibromatosis was made and confirmed by Dr. A. Rostenberg.

The most frequent fibroma of the skin occurring in multiple form is the so-called fibroma molluscum. von Recklinghausen,[1] in 1882, showed that this tumor arises from the cutaneous nerve filaments, a conclusion which had been suggested by some previous writers and verified by many later studies. He traced degenerating nerve fibers in several characteristic cases and stated that all these tumors arise from nerve-trunks or filaments.

Hirsch[2] reported a case of neurofibromatosis in a female, age 37, becoming worse during the seventh month of her first pregnancy, which soon after the termination of that pregnancy underwent a process of remission.

Nishizaki[3] cites a case of von Recklinghausen's disease occurring in a married woman 22 years old, with a history of pigmented spots present since the age of six. In the third month of her pregnancy these were noticed to increase in size and number. In the fifth month after labor the tumors faded and decreased. But when she was pregnant for the second time the process repeated itself.

Wise and Eller[4], in reviewing the literature on von Recklinghausen's disease, cite Feindl, who reports a case of neurofibromatosis first appearing at time of childbirth.

Rosensohn[5] reported a case of von Recklinghausen's disease in the Bulletin of the Lying-In Hospital. He pointed out that any procedure which becomes a routine may ignore features which make every case interesting.

In presenting these cases, the desire has been to stimulate the thorough examination of every patient—even those seen on a maternity service. The obstetrician must not be satisfied with the idea that a mother can have no other abnormality than one connected with her pregnancy. The histories noted in this article are given in detail because of the dearth of reports showing the association of the two conditions.

I wish to express my thanks to Dr. Meyer Rosensohn for permission to publish these cases; and also to Miss Dora Laks, historian of The Bronx Hospital, for her aid in obtaining these records.

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A CASE OF INTRAABDOMINAL HEMORRHAGE FROM RUPTURE OF A UTERINE VEIN DURING PREGNANCY

By Henry C. Falk, M.D.,* New York, N. Y.

I WISH to report a case of intraabdominal hemorrhage resulting from the spontaneous rupture of a uterine vein during the sixth month of pregnancy, with operation and recovery.

Mrs. I. C., age 27, was admitted to the service of Dr. Charles Hyman at the Beth David Hospital on January 25, 1929, and gave the following history: Seven hours before her admission to the hospital she rose from a chair and was seized with a sharp excruciating pain radiating from the vulva to the umbilicus along the anterior abdominal wall. She was carried to bed and soon began to complain of faintness, dizziness and blurred vision. She vomited twice before admission. Her symptoms persisted, she became dyspneic and went into a state of partial shock. Temperature 97.6, pulse 116, respirations 22. Physical examination of the lungs showed normal pulmonary resonance to percussion, breath sounds were vesicular throughout, there were no râles present. The heart was not enlarged, apex palpable in the fifth interspace within the nipple line, sounds of good quality, there was a slight systolic murmur at the base, not transmitted. Abdominal palpation revealed tenderness and slight rigidity over both lower quadrants. The uterus could be palpated extending just above the umbilicus. Fetal parts seemed prominent. Shifting dullness was elicited over both flanks. The abdomen was distended and typanitic throughout. Vaginal examination revealed a softened cervix, admitting the finger tip, no tenderness in the culdesac, no tenderness in the fornices. Bimanual examination revealed the size and location of the fundus corresponding to abdominal palpation. Any movement of the cervix or uterus caused severe pain. On withdrawing the examining finger no evidence of free or clotted blood was seen. A blood count showed 18,200 white blood cells; polymorphonuclear leucocytes—85 per cent, mononuclear cells—15 per cent, hemoglobin 40 per cent, red blood cells 1,900,000. The urine was amber colored, specific gravity 1.017, acid in reaction, albumin negative, sugar negative, acetone negative, microscopic examination revealed a few round bladder cells, a very occasional red blood cell, no pus, no casts. The blood pressure was 96/60.

Owing to the apparent prominence of fetal parts, signs of severe hemorrhage, and the presence of fluid in the abdomen a preoperative diagnosis of spontaneous rupture of the uterus was considered, but as there was no previous history nor any condition which might have caused a weak uterine wall, it was discarded. Pre-

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mature separation of the placenta was thought of, but there was no evidence of vaginal bleeding and the symptoms indicative of possible extrauterine hemorrhage could not be overlooked. Preoperative diagnosis: intraabdominal hemorrhage, etiology unknown.

Under gas-oxygen-ether anesthesia a low midline incision was made. The peritoneal cavity was opened, the uterus drawn forward, and a large quantity of free blood found, partially clotted, filling the entire abdomen. The blood was removed and the abdomen explored for possible source of hemorrhage. The uterus looked apparently normal. The spleen was found intact, there was no sign of hemorrhage from the liver, kidneys, omentum or mesentery. Reexamination of the uterus showed on the posterior surface close to the left broad ligament, a small opening about 4 mm. in diameter. The area presented a punched-out appearance, and at its lower edge a small blood clot was found adherent. On removing this clot a small amount of blood escaped. Not recognizing the true pathology of this condition, a supravaginal hysterectomy was performed.

The patient was transfused with 800 c.c. of whole blood, Lindermann method.

The patient's convalescence was normal and she left the hospital in sixteen days.

The specimen was opened and found to contain a live six months fetus which expired almost immediately. The placenta which was attached on the left side close to the fundus posteriorly was removed and showed no evidence of concealed intrauterine hemorrhage. The eroded area was probed and found to enter a collapsed, thin-walled vein. Postoperative diagnosis: Rupture of a varicose vein of the broad ligament.

These cases are extremely rare. A search of the various obstetric and gynecologic textbooks revealed no mention made of this condition as a complication of pregnancy.

Of the twelve cases reported in the literature nine represent autopsy records: Langes, Teller, Leopold, Kaufmann, Chaussier, Fritsch; two cases, those of Williams and Teller, were pelvic hematomas. Three cases, those of Miller, Halban and Modiano, were operated on and recovery ensued. In Miller's case, the preoperative diagnosis was premature separation of the normally implanted placenta with concealed hemorrhage and a classical caesarean was performed; living child, died in a few hours. In Modiano's case the preoperative diagnosis was spontaneous rupture of the uterus. A classical caesarean was performed, living child, died on fourth day. In Halban's case the preoperative diagnosis was perforation of the uterus and a vaginal hysterectomy was performed (three month pregnancy). This makes the fourth case operated on (hysterectomy) with recovery.

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1 West Eighty-sixth Street.

HEMORRHAGE INTO HYDATID OF MORGAGNI SIMULATING ACUTE APPENDICITIS

By Abraham Heinrich, M.D., Brooklyn, N. Y.

(From the pathological laboratory of Brownsville and East New York Hospitals)

HYDATIDS of Morgagni, embryologic rests of the wolffian duct, are of frequent occurrence, as seen both at the operating table and in the postmortem room. To these cysts, clinical symptoms are rarely attributable. A few cases are on record wherein the cysts grew large enough to be palpated and require surgical intervention. Still more uncommon is the accident whereby torsion of the cyst occurs simulating clinically the picture of an acute abdominal disturbance. In a careful survey of the literature extant, we have been able to discover but three other reported cases, to which we should like to add one recently coming under observation.

CASE REPORT

M. S., aged fifteen, well developed and giving an irregular menstrual history. Her menses began at fourteen years of age with a duration of eight days, and for the first four times occurred every two weeks. Following that they occurred every six weeks. Her periods were accompanied by lower abdominal cramps on the first day. Her last period occurred about two months before the onset of her present illness and lasted for three days.

On the day before admission to the hospital, the patient began to complain of mild lower abdominal cramp-like pain. The pain became more intense and the next day toward evening she vomited several times. There was no constipation. Physical examination revealed definite tenderness over McBurney's point; pulse 92, respiration 26, and temperature 100.8° F. by rectum. A rectal digital examination revealed marked tenderness in the right pelvis. On admission to the hospital, her blood count was 9200 white blood cells, of which 80 per cent were polymorphonuclears. Her urine was negative.

A laparotomy was performed the same evening. Through a McBurney incision the appendix was visualized and found grossly normal. A dumb-bell-shaped black mass was found hanging from the fimbriated end of the right tube. Each half of the mass had a base of 1 cm. in diameter and was 1 cm. high and the two tips were joined by a short, narrow strand which showed one complete twist. Both ovaries were slightly cystic, the tubes were normal. The mass was ligated at its site of attachment and removed. The abdomen was closed without drainage. The patient made an uneventful recovery. On microscopic examination:

1. The appendix was found normal.

2. The cyst was lined by a single layer of very low cuboidal cells beneath which was poorly staining smooth muscle. Many necrotic vessels, some hyalinized, and groups of polys and hemorrhage were present in the wall. The contents of the cyst were composed of red cells together with an eosin staining amorphous gelatinous material.

Her next menstrual period occurred two and one-half months after her previous one, nineteen days after onset of symptoms and eighteen days postoperative, ac-

companied by severe lower abdominal cramps on the first day. The following period occurred two months later and was not accompanied by pain. Both lasted three days with moderate flow.

REVIEW OF LITERATURE

Andrews'[1] case was that of a woman, thirty-six years old, pregnant six months, giving a history of pain in the right lower quadrant, aggravated by fetal movements. There was no vomiting. She was comfortable for a week but tenderness was present above and within the anterior superior spine on the right side. She became distended and the pain increased in severity. Operation revealed a small purple body the size of a grape (4 cm. × 1.5 cm. and constricted in its midportion) hanging from the fimbriated end of the right tube. Both tubes and ovaries and the appendix were normal. The pathologic report revealed lymph on the surface of a thin-walled cyst filled with a blood clot.

Waters'[2] case was that of an eighteen-year-old single girl complaining of pain in the left lower quadrant with severe vomiting. Her temperature was 101°, pulse 130, 16800 white blood cells of which 86 per cent were polymorphonuclears. The menstrual cycle was of the three-week type accompanied by dysmenorrhea. She gave a history of several attacks of similar pain in the preceding nine months. She was kept under observation for five days and when operated upon, blood tinged serous fluid was found in the abdominal cavity and, hanging from the left tube by a pedicle 2.5 cm. long, and showing one complete twist, was an hydatid of Morgagni the size of an olive, about 2.5 × 2 cm. Both ovaries were cystic, the appendix was normal.

Abernethy's case[3] was that of a married woman aged thirty-three, grava iv, para iii, who gave a history suggestive of an incomplete abortion following a two months' period of amenorrhea. She then had pain in her right lower quadrant with vomiting for three days. Her temperature was 99.4° F., her pulse was 80. A "dilatation and curettage" and a laparotomy was performed with the following findings: (1) Products of conception. (2) An old chronic appendicitis. (3) A hydatid of Morgagni 2 cm. × 7 × 7 cm. hanging from the right tube, reniform in shape and showing two twists. The serosal lining was thick and lusterless. A smaller cyst was present on the left side. (4) Bilateral small ovarian cysts.

In an analysis of the few recorded cases, the age incidence in both Waters' and our cases fell in the second decade. Both are single adolescent girls. Andrews' and Abernethy's cases occurred in married pregnant women in their "thirties."

The menstrual history was not given in Andrews' or in Abernethy's cases. Waters' and our cases gave very irregular menstrual histories.

Waters' case had pain in the left lower quadrant. There was no radiation of the pain in any of the cases. Andrews' patient did not vomit, the other three did. The temperature and pulse were variable from 101°, pulse 130 to 99.4°, pulse 80. Andrews' does not give the pulse nor temperature. The blood count of Waters' case was 16800, 86 per cent polys, ours was 9200, 80 per cent polys. The other two are not given.

Waters' case had a twisted hemorrhagic hydatid of Morgagni hanging from the left tube, the three others were hanging from the right tube. Abernethy's case had a chronic appendix. All the other three had

normal appendices. The ovaries of Andrews' case were normal. The ovaries of the other three were cystic. Waters' case had a pedicle 2.5 cm. long and twisted twice. The other three had no pedicle. Andrews' was constricted in the midportion. Abernethy's was reniform and had two distinct twists. Ours was dumb-bell shaped and had one complete twist.

SUMMARY

These cases illustrate the similarity of the clinical picture of twisted hemorrhagic hydatid of Morgagni to that of an acute appendiceal lesion. The former however gives a history of a menstrual irregularity and dysmenorrhea (our attack occurred before the onset of menstruation), with only a few of the signs of an acute abdomen.

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4600 Fourteenth Avenue.

A CASE OF CHRONIC MENORRHAGIA CURED BY GALVANIC DILATATION AND ZINC CHLORIDE IONIZATION*

By Victor C. Pedersen, A.M., M.D., F.A.C.S., New York, N. Y.

A. M., U. S. A., white, twenty-seven years old, married, housewife, first seen February 22, 1926.

Diagnosis.—Chronic relapsing menorrhagia complicated by nongonococcal acute vulvovaginitis and acute vulvovaginal abscess.

General health and habits good. Constipation moderate. Venereal history negative.

Menstruation began at fourteen, no pain, but irregularity and excess great, so that flow appears at unknown intervals and sometimes continues for two or three weeks until going to bed stops it. For about seven years, therefore, she has been a victim of easy chair or bed life many months in the year and for long periods of those months. One of the mysteries of this case is how she compensated for this loss of blood and strain on the nervous system. When I first saw her she was and remained a rosy cheeked, quietly disposed, attractive girl.

Another mystery is how this girl ever considered herself marriageable in the face of such an infirmity. She did not let her fiancé know anything about it until after marriage.

Her sexual instincts and their gratification are normal, except for their early marital excesses as hereinafter stated.

Her present sexual history is very instructive. She is the wife of M.P.M., whose first and divorced wife also had a double standard consisting in practical absence of sexual instinct and denial of nearly all sexual intercourse.

The usual result followed. The husband was compelled to practice his own double standard, and acquired gonorrhea.

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*Read before the Section on Obstetrics and Gynecology of the New York Academy of Medicine, April 22, 1930.

Marriage was permitted only after six months of freedom from all symptoms and after many smear, culture, and seven glass tests were consistently negative for the gonococcus or other pathogenic organisms. The marriage occurred thirty-nine months after the treatment stopped, during which time he remained free of subjective and objective symptoms. His last test was a short time before marriage according to my advice and custom.

Intercourse was excessive to a very high degree. Lysol douches were used as contraceptives and although weak, induced a purulent vulvovaginitis in a few days followed by abscess of the left vulvovaginal gland.

The bacteriologic investigation was by smears and cultures from the urethra, vulvovaginal gland outlets and vulva as a whole, posterior culdesac of the vagina, and the cervix. Its findings were negative for the gonococcus, positive for the bacillus coli, diphtheroid group, and many pus cells. Many nonspecific bacilli were found.

The behavior of the discharge was that of gonococcal infection except the color, odor, and consistency of the pus. The patient admits the peculiar habit of wiping herself after defecation toward the vagina instead of away from it. This fact probably introduced the bacillus coli into the vulva and vagina as a complicating infection. Careful instructions were given to avoid this infection.

The specimens were taken by pressing the swab to squeeze mucus out of the glands. This detail seems to be neglected because in my work for one of the institutions for unmarried mothers I have regularly found positive smears from time to time in young women coming from nearly every hospital in Greater New York, with reports negative for the gonococcus. Moreover, the four anatomical points I have named do not seem to be systematically examined by taking an original and a control specimen. Too much caution cannot be exercised.

The treatment was at first against the infection and next against the chronic menorrhagia.

Normal salt solution douches were substituted for the lysol, four times a day as hot as tolerable and as a contraceptive. Office douches of 1 in 8000 slowly ascending to 1 in 4000 formalin were given to kill off the bacillus coli, which occurred in about three weeks. The vulvovaginal abscess was at first treated with 10 per cent ichthyol salve but was finally lanced and evacuated of 30 c.c. of bloody pus. It healed, leaving only a small node, in about three weeks.

The disappearance of pus in about sixty days permitted attention to the uterus.

As a means of hemostasis and ovarian control two roentgen-ray treatments were given 60 milliampere minutes each, from the static machine, with a tube backing up a 5″ spark gap. The distance was 8 inches. The filter was ⅜″ sole leather and 3 mm. of aluminum. First one ovarian region then the other was rayed, including the uterus each time. At the end of all treatment one more x-ray treatment was given. Radiant light followed the x-ray (one visit later from field to field) to protect the skin.

As a means of restoring the pelvic circulation to balance, diathermy was tried ranging from 500 to 1500 M.A. employing 8 inch by 10 inch electrodes beneath the buttocks and over the pubes. Contrary to expectations this very mild current seemed to excite the bleeding. It was not repeated. It should be remembered that such a current between such large electrodes is mild. In this case the patient perceived a gentle warmth. The actinic influences (though not felt by the patient) are more important than the warmth noticed by the patient.

Galvanic dilatation of the cervix for drainage up to ⅜ inch with the negative pole in the cervix and distributing plates on the buttocks and pubes (and well lapped upon the sides) was employed. Next the cavity of the uterus was packed with fine gauze strips soaked in 10 per cent chloride of zinc solution tied to the

vaginal packing, retained twenty-four hours or less, then removed by the patient and normal salt solution vaginal douches employed.

The zinc chloride packings were used once a month. The galvanic dilatation was also a zinc ionization and repeated every four, seven, and fourteen days. After the cervix had dilated and relaxed under the negative pole the polarity was changed to positive for five minutes so that zinc ionization would occur. In order to avoid adhesion to the positive electrode, the polarity was again changed to negative for about five minutes. All these currents were very mild, never above 10 M.A., and always comfortable to the patient. Zinc chloride 10 per cent was applied to erosions of the cervix at each visit, with benefit.

Improvement in the discharge began with the fifth galvanic treatment (within eleven days). The bleeding from the uterus also decreased. The treatment was continued from May 10 to September 29 at increased intervals up to once in about fourteen days. There were only three visits in September, 1926.

She was next seen in December, 1926, examined, found in good condition. One dilatation treatment was given.

In March, 1927, she called to report a slight relapse. This was certainly due to very unreasonably excessive intercourse which was immediately forbidden on the ground that such sexual strain would reinduce the ovarian and uterine functional disorder. One dilatation with zinc ionization was given followed by static wave current to the uterus to compel its return to tonicity. This treatment was efficient the sufficient because she did not return until September, 1927, with this report: discharge moderate, no napkin used, no stains on clothing. In fact she was free from discharge until three weeks previously when slight relapse occurred, ranging from few streaks to enough to annoy. Menses normal within the average for all women. Coitus normal in frequency and without pain. Contraceptives: normal salt solution douches only. At examination normal in all respects. Discharge a typical, simple, moderate leucorrhea.

Last seen June 20, 1929, about three years after beginning treatment. Menses nearly painless, normal quantity and duration, nearly normal intervals. At times has flowed for about one week. Leucorrhea present but not severe. Coitus about 2 times per week, not painful. The vulva and vagina were clean. Cervix was very slightly eroded. Uterus soft.

On account of the erosions and softening another course of treatment was begun. Only two dilatations and zinc ionizations seem to have relieved the status.

The couple was warned that a functional disorder of at least seven years' standing must leave behind it a definitely weak spot anatomically and physiologically speaking, which will respond by relapses to such causes as exposure to cold and wet, bodily strain as in long automobile rides, excessive intercourse and wrong douches in terms of temperature and chemical substances. Advice to omit all contraceptives, reduce intercourse to once in seven to ten days, invite and accept pregnancy as the best possible physiologic cure has so far been ignored and probably will be ignored.

CONCLUSIONS

1. Good health maintained for seven years during such loss of blood as this woman had is rare.

2. The prompt incidence and the consistent progress of benefit by electrotherapeutic means need hardly more than mention to be impressive and convincing.

3. One leading gynecologist of this city has already admitted to one of my colleagues in electrotherapy that he should do more office work with physical measures and less operative treatment.

4. When the value of physical measures becomes common property many operations now being done will be refused, as they should be refused, at least until said measures shall have been skillfully and perseveringly tried and failed.

5. This patient was cured without the costs of absence from home duties, of hospitalization, of surgical and nursing fees and without the risks of anesthesia and operation. Results of this kind are not medical curiosities but rather common experiences in skilled hands.

45 West Ninth Street.

A RACHITIC NAEGELE TYPE PELVIS WITH FAULTY INCLINATION AND MARKED SPINAL DEFORMITY*

By J. Bay Jacobs, M.D., F.A.C.S., Washington, D. C.
(Associate Clinical Professor of Obstetrics, Georgetown University)

A COLORED woman, gravida i, twenty-three years of age, was first seen in the prenatal clinic of Georgetown University Hospital, September 10, 1928. Although her gait was normal, the unusual prominence of her buttocks attracted attention. Examination of her back in the standing posture showed the depression denoting the right sacroiliac synchondrosis to be about 1½ inches higher than the left. A lumbar lordosis with a left scoliosis was very evident. A marked right scoliosis of the dorsal vertebrae and a compensatory left scoliosis of the upper dorsal and cervical vertebrae was noted. The external pelvic diameters were as follows: Interspinous 26, intercristal 23, external conjugate 15.5, right oblique, 18.5, left oblique 20+.

With the aid of my obstetric inclinometer, it was found that the symphysis was 6 cm. high, the diagonal conjugate 9 cm. long, with the promontory located to the left of the midline. Conjugate of outlet was 8.5 cm. and bituberal diameter 10.5 cm., calculated true conjugate 8.5 cm. Diagnosis of Naegele type rachitic pelvis with spinal deformity. Although the left oblique diameter was larger than the right, a favorable prognosis was predicted, should the patient have a small baby and the head select the right oblique diameter, especially as an R.O.P., because of the situation of the promontory on the left side. The brim appeared flattened on the left side, which further tended to diminish the available space at that half of the inlet.

Usual prenatal care was given and at 11 P.M. March 5, 1929, patient entered hospital in labor. Examination two hours later revealed fundus at ensiform with small parts in R.U.Q., head floating and F. H. 145 to the left and above the navel. An attempt at manipulating the abdomen in order to rotate the occiput to the right side was unsuccessful. After twenty-four hours of labor with no engagement, a transperitoneal cesarean section was done. Before closing the abdomen the true conjugate was measured directly with an accurate scale, and found to be 8.5 cm. The living male child weighed 5 pounds, 9 ounces.

Postpartum hemorrhage occurred six hours after operation and the husband who was informed of the urgent need of transfusion, refused to obtain a professional donor until the next day when the patient was moribund. Death occurred and at postmortem examination there was no blood found in the peritoneal cavity

*Demonstrated before the Georgetown Clinical Society April 17, 1930.

and the pelvic organs were negative. The pelvis and part of the spinal column were removed as shown.

DESCRIPTION OF SPECIMEN

The pelvic inlet is flattened on the left side anteriorly, the right sacrocotyloid diameter measuring 8 cm. and the left 6.75 cm. The distance from the center of the promontory to the right sacro-iliac synchondrosis is 6 cm.; the corresponding measurement to the left is 5 cm. The distance from the promontory to the middle

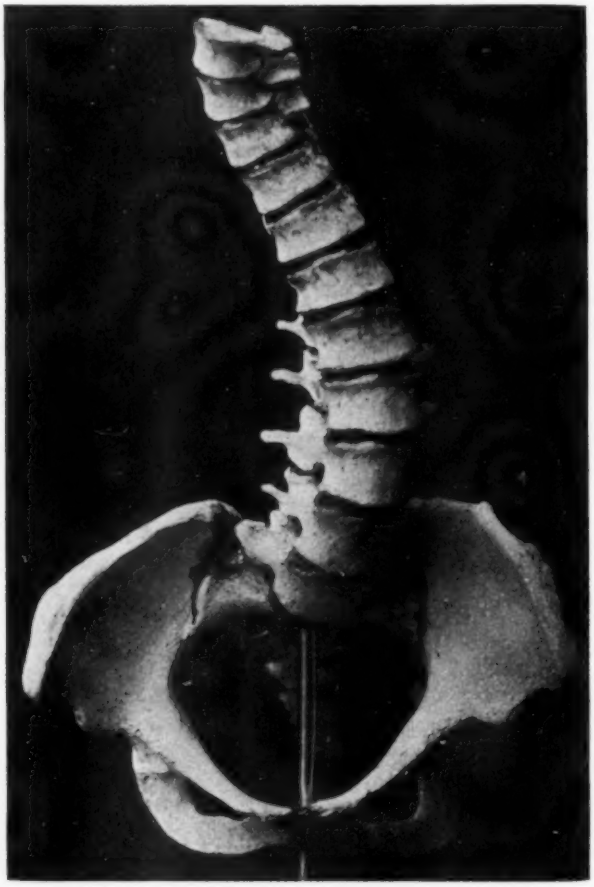

Fig. 1.—Anterior View. Shows flattening of left side of brim and faulty inclination. Interspinous diameter is greater than intercristal and iliac fossae look forward. The anterior surfaces of the lumbar vertebrae are directed toward the left and the dorsal are directed toward the right. Lumbar lordosis evident. Left sacral ala is smaller than the right.

of the upper border of the symphysis which with the aid of the inclinometer was found to be 8.5 cm., measures 8.25 cm. on the dried specimen. The diameter from the promontory to the inner margin of the upper border of the symphysis measures 7.7 cm. The left oblique of the superior strait is 10.5 cm. and the right oblique 9.75 cm. Although the left sacral ala is smaller than the right it is well formed, and the articulation with the iliac bone is normal. The entire pelvis is rotated on a transverse axis running through the sacroiliac synchondroses, and the habitual inclination is almost 90 degrees, for the inlet is practically perpendicular to the

horizon. The iliac bones as shown in Fig. 1 are not symmetrical, the crest of the right one extending outward about 1.25 cm. more than the left. The interspinous diameter measures 25 cm. and the intercristal 23 cm. The iliac fossae look almost directly forward.

Inspection of the posterior aspect affords an excellent view of the outlet. The arch is extremely wide and shallow, the anterior sagittal measuring 4.25 cm. and the transverse of the outlet well over 11 cm. The left pubic ramus is smaller than the right and the edges of both are markedly everted. The left ischial spine

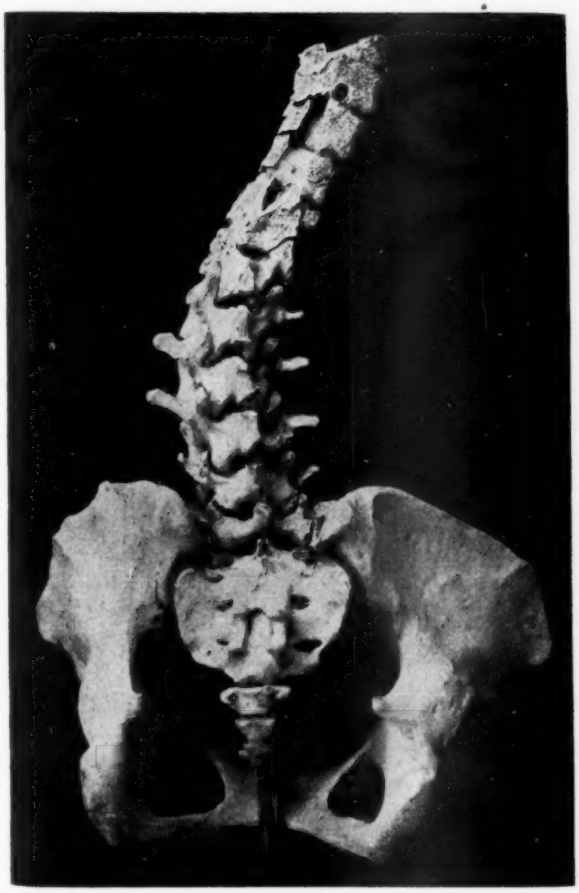

Fig. 2.—Posterior View. Shows position of sacrum, the wide shallow arch and rotation of entire pelvis on a transverse axis running through the sacro-iliac synchondroses. The transverse processes vary in size.

is larger and thicker than the right. The internal surface of the sacrum looks directly downward and the posterior surface almost directly upward, the sacro-coccygeal joint being situated 8.25 cm. behind an imaginary perpendicular line running through the posterior margin of the upper border of the sacrum. The distance of the posterior superior spine of the right iliac bone to the posterior surface of the sacrum measures 2.5 cm., the corresponding one on the left measuring 3.2 cm. The sacral foramina are irregular in size and shape.

The vertebral column was mounted in its normal attitude, the spinal curvatures being clearly shown in the illustrations. There is a marked lumbar lordosis,

especially of the last two lumbar vertebrae, with a left scoliosis. These vertebrae appear to be rotated on a vertical axis so that the anterior surfaces are directed toward the left. In the dorsal region there is a scoliosis to the right, with a marked rotation of the vertebrae, so that their anterior surfaces look toward the right. On all the vertebrae and in each individual bone, the transverse processes vary in size and thickness. The lordosis and the unusual position of sacrum are well shown in a lateral view.

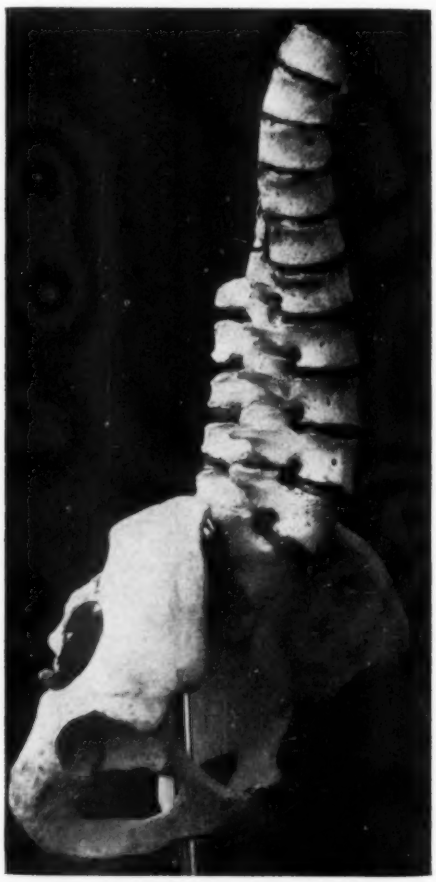

Fig. 3.—Anterolateral View. Showing marked lumbar lordosis, the rotation of bodies of vertebrae on their vertical axes, and the unusual relation of the pelvis to the spinal column.

CONCLUSION

In this particular case there was no marked disproportion between the inlet and the fetal skull. The lumbar lordosis besides limiting greatly the available area at the inlet, would direct the presenting part over the upper border of the symphysis instead of into the pelvis. It would be impossible for the birth object to round this great curve and enter an inlet of such faulty inclination.

CHASTLETON HOTEL.

MONO-AMNIOTIC TWINS WITH TWISTED CORDS*

By Tiffany J. Williams, M.D., Great Falls, Mont.
(From the Division of Obstetrics and Gynecology of the Great Falls Clinic)

THE infrequency of reported cases of mono-amniotic twins with twists and knots of the two cords, would seem to justify a report of the following case.

Mrs. J. Z., aged thirty, had previously had two full-term normal pregnancies and one miscarriage at three months. The previous menstrual history was normal and of the regular twenty-eight day type. There had been no past serious illnesses or operations.

The last menstrual period occurred on Nov. 15, 1928, since which time there had been no nausea or vomiting although occasional frontal headaches had been present. Fetal movements were noticed from April until July 1, 1929 when the movements ceased. On July 9, 1929 the patient was referred to the Deaconess Hospital after having been told by the attending physician that the baby was dead.

Fig. 1.—Photograph of the placenta and the knotted cords from a case of mono-amniotic twins.

The general physical examination on admission revealed essentially normal findings. Abdominal examination showed the fundus of the uterus to be about nine cm. above the umbilicus. The uterus was tensely distended by an excess of amniotic fluid so that no fetal parts could be palpated and the fetal heart could not be heard. The urine examination was normal, blood pressure was 120/80, and the blood Wassermann test was later reported as negative.

Labor began spontaneously on July 9, 1929, and after four hours of labor pains, the cervix was fully dilated. The membranes were ruptured artificially, and a still-born macerated female infant was born spontaneously ten minutes later. The cord of this infant was stretched so tightly that it had to be clamped before the body could be completely delivered. Examination revealed the presence of a second infant, and ten minutes later, another macerated female child was born without difficulty. Immediately following the birth of the second child a knot of cords approximately the size of a man's fist escaped from the vagina. The placenta separated spontaneously and was expressed intact from the vagina a few minutes later.

Both infants were macerated females, weighing 1750 gm. and 1825 gm. respectively. The placenta weighed 650 gm. and measured 22 cm. × 17 cm. × 3 cm. The cords, which were 6 cm. apart, were eccentrically inserted, one 3 cm. and the other 4 cm. from the edge of the placenta. There was an anastomosis of the

vessels of the two cords on the fetal surface of the placenta. The membranes were ruptured 6 cm. from the edge of the placenta and consisted of a single chorion and a single amnion. No evidence of the remains of an amniotic partition could be found.

At a distance of 15 cm. from the placenta the two cords were twisted and looped tightly around each other, forming a knotted mass the size of a man's fist. The cords were of a dark hemorrhagic color and measured in length 45 and 52 cm. respectively.

DISCUSSION

The present case is undoubtedly one of mono-amniotic twins, in whom the cords were twisted and looped around one another tightly enough to occlude the circulation in both cords, resulting in the death and premature delivery of both babies.

Sonntag in 1905 collected 23 cases of mono-amniotic twins from the literature and discussed the etiologic theories of their production. There are in general two theories advanced to explain the production of single amnion twins, either two amnions originally develop, and, as a result of a tear in the adjacent amnions, the cavities are united, the torn partition being subsequently absorbed, or it is assumed that two embryonal areas develop in close proximity, so that one amnion may encircle both embryos. Dancing, horseback riding, vomiting, and falling, as well as hydramnios and excessive length of the cords have been considered as predisposing causes for the looping and twisting of the two cords.

In examining the literature I have been able to find additional cases reported by Plitz, Pallin (2 cases), Roberg, Vallois L., and Vallois H., Dietrich, and Abrams, making a total, including the present case, of 31 reported cases.

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A CASE OF UTERUS UNICORNIS WITH RUDIMENTARY LEFT UTERUS AND RIGHT ECTOPIC PREGNANCY

By Dean W. Hart, M.D., St. Johns, Mich.

THIS case is of interest because ectopic pregnancy occurred in a pelvis also containing a rare form of uterine anomaly. Reading of the following history and physical examination records makes further comment unnecessary about the value of thoroughness in examination and history taking.

Mrs. A. M., a patient of Dr. Frost C. Buchtel, August 17, 1929. The father is one of fourteen children, all his married sisters having normal children. Two unmarried sisters are apparently normal. The maternal grandmother is one of twelve children. The mother has one brother and one sister, both of whom have children who are apparently normal. Fifteen years ago the mother had a hysterectomy, laboratory report being sarcoma, but she is healthy today. No pelvic abnormalities were noted. The mother's first child was a premature macerated stillbirth. Her second child, also prematurely stillborn, had one clubfoot and hydrocephalus. Her third child was also stillborn, but was apparently normal. The patient is the fourth child and there was a healthy son later.

The patient is twenty-five years old, married eighteen months, with normal sex life.

Her only serious illness was rheumatic fever at ten years of age.

At the age of thirteen she menstruated once. A year later her periods started again and have remained normal and regular through June 25, 1929.

Chief Complaints.—Abnormal vaginal bleeding; nausea and vomiting; pain in right lower quadrant.

On July 4, she began to have excessive vaginal bleeding which lasted three weeks accompanied by almost continued nausea and vomiting, right lower abdominal aching and colicky pain. After several days of relief, the symptoms returned. At this time the vomiting attack was followed by distention. She noticed a painful lump in one breast. She was studied by three New York City doctors during this time, all of whom diagnosed the trouble appendicitis. No vaginal examinations were made, but there were many blood examinations. During a second intermission of symptoms, the patient started for Denver, becoming ill again on the train. One attack of pain was so severe that she fainted. There have been no chills or fever, and no symptoms referable to lungs, heart, kidneys or gastrointestinal tract.

Examination.—The patient was markedly pale and weak. In the abdomen there was tenderness over the appendix. No rigidity, distention, or masses were noted. The vaginal examination disclosed an enlarged and tender right tube. The right ovary was also enlarged. Left adnexa were negative. The uterus was in the axis of the vagina, was normal in size and was, perhaps, a little softer than normal.

Laboratory Findings.—Leucocytes, 9,200; Hb, 82 per cent; red cells, 4,080,000. Urine was negative.

Diagnosis.—Probably right extrauterine pregnancy. Postoperative diagnosis: Same.

Operation.—Low midline incision; abdominal cavity contained nearly a quart of bloody fluid and clots. The right tube was enlarged and the point of rupture was about an inch from the proximal end. The right ovary was normal. It was then discovered that there was an absence of the left uterine cornu. However, lying

between the layers of the broad ligament, three inches to the left of the uterus, was found a symmetrical oval-shaped rudimentary uterus the size of an English walnut. Embedded in the left lateral wall of this uterine body was the normal left ovary, and adherent to this was one-half inch of the fimbriated end of the left tube. The normal left round ligament was attached to this rudimentary uterus. After careful examination no connection was found either between the fimbriated end of the left tube and the rudimentary uterus or between the rudimentary uterus and the main uterus or vagina. This anomalous condition was left intact because removal of the extra uterus would have endangered the blood supply of the ovary. After removal of the right tube and the appendix the incision was closed. The convalescence was uneventful.

It would appear that this anomaly resulted from nondevelopment of the lower half of the left muellerian duct with complete failure of fusion of the muellerian ducts. Since there was no actual connection between the rudimentary uterus and rudimentary end of the oviduct, there must have been also a failure in development of the midpart of the upper third of the left muellerian duct. The left ovarian ligament was absent, but the position of the ovary with the rudimentary uterus in-

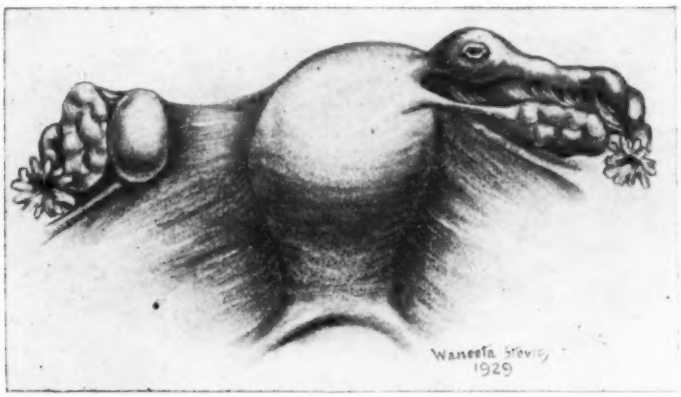

Fig. 1.

dicated that its original function of bringing the ovary into the pelvis was fulfilled.

Although a careful search of the literature available has been made, no example of this anomaly has been found. Neither has the title of any unavailable English article a suggestion that it presents such a case.

Hill and Newton both reported cases in which there was a perfectly formed rudimentary uterus lying in the broad ligament, but which had a small fibrous cord running out along the lateral pelvic wall to connect with the normal uterus at the cervix or even connecting with the vagina. Hill says that such a fibrous band may be so small as to escape macroscopic notice during life. However, he neither gives a bibliography nor cites cases in which this has occurred. Furthermore, the anomaly under discussion was not at all a perfectly formed rudimentary uterus.

A case mentioned by Fromell, of Germany, in 1890 was similar. The only difference was that there was also a rudimentary horn in normal position which had a blind end a short distance from the uterus.

In reading literature on anomalous uteri, it is interesting to notice that a great number of titles of American articles fail to signify much about the context. The foreign articles are, as a rule, better named.

SUMMARY

In this case a complete physical examination in conjunction with a carefully taken history of the present illness, made possible a correct preoperative diagnosis of ectopic pregnancy, although three surgeons had previously diagnosed appendicitis, having neglected to make a vaginal examination. The anomaly, however, was not recognized preoperatively. The rudimentary uterus, three inches to the left side of the normally situated uterus was interpreted as the left ovary. This failure well illustrates the extreme difficulty of making an absolutely correct preoperative diagnosis in a pelvic or abdominal case.

The anomaly found was uterus unicornis with a small left-sided rudimentary uterus. No case identically the same was found in the literature.

204 WEST STATE STREET.

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PREGNANCY IN UTERUS BICORNIS UNICOLLIS WITH THE CHILD OCCUPYING ONE HORN AND THE PLACENTAL SITE A PORTION OF BOTH

BY WILLIAM A. MICHAEL, M.D., PEORIA, ILL.

THIS case is reported because it presents a number of features commonly associated with pregnancy and labor complicated by bicornate uterus, together with a rather unusual feature, namely, the attachment of the placenta at the juncture of the two horns so that the placental site occupied a portion of both. Prior to labor, findings were insufficient to justify more than a probable diagnosis of bicornate uterus, and the true condition remained unrecognized until the interior of the uterus was explored attending placental removal.

Case Report.—Mrs. A. L., white, aged thirty-five, presented herself two years ago for investigation of sterility. She had never been seriously ill, and had had no operations. Her menstrual periods had been normal since onset at fourteen years, and although married for ten years, she had never conceived. Owing to retrocession it was not possible to palpate the uterus in its entirety, but otherwise no abnormalities were disclosed, and she was, from a general standpoint, physically fit. The Huhner test proved normal, but in performance of the Rubin test, gas failed to pass at 200 mm. of Hg. A later tubal insufflation, to be followed by a hysterogram, was advised, but was indefinitely deferred by the patient.

She again came under observation on July 16, 1929, her latest menstrual period having occurred on May 30, 1929. At this time it was impossible to outline the corpus, but the softened cervix and lower segment, together with the subjective symptoms, left little doubt as to the existence of pregnancy. Examination on September 3, 1929, showed the uterus nicely forward, size of ten to twelve weeks, and no apparent abnormality. Except for "spotting" on June 27 to 30, rather free bleeding for twelve hours, without pain, on October 25, and slight bleeding on November 11, 1929, the pregnancy pursued a normal course.

On January 9, 1930, eight weeks in advance of expectancy, the membranes ruptured without warning, and the patient entered the hospital. There was an unusual broadness of the fundus without demonstrable notch between the two sides and without torsion. A fetal pole, which on rectal examination was considered cephalic, presented in upper pelvis. That the deformity of the fundus was due to myoma was considered highly improbable owing to earlier observation. This left fetal or uterine malformation for consideration, and the former was definitely excluded by x-ray which revealed the breech presenting in L.S.A., but failed to explain the broadening of the fundus.

Labor set in ten days later and pursued a slow, tedious course; the contractions were weak and ineffectual, and eventually required the administration of morphine and chloral for periods of rest, on two occasions. The fetal heart tones remained regular throughout, at a rate between 130 and 140. After cervical

Fig. 1.—Hysterogram showing uterus bicornis unicollis and right tubal patency. The area between points *A* and *B* indicates, relatively, the former placental site.

effacement, as followed by rectal palpation, was finally accomplished, a hydrostatic bag was inserted, and dilatation secured in a few hours. Following expulsion of the bag, the breech was spontaneously born and extraction was made without difficulty.

After delivery, the fundus showed a distinct notch which divided the uterus into a large left portion and a lesser right, the latter being approximately 15 cm. across. In the usual period of time there were no signs of placental separation, and efforts at expression were unavailing. The Mojon-Gabaston method of umbilical vein injection with saline was tried without effect. Invasion of the uterus, after the membranes had been ruptured for so long a period, for the manual removal of the placenta admittedly entailed a considerable risk, yet the deformity of the uterus and the prematurity of the labor seemed somewhat against normal separation, and certainly, later removal would be extremely hazardous. Accordingly, two hours after delivery, the placenta was manually removed without difficulty and without unusual hemorrhage. The following condition was noted: In the region

of the right horn, a distinct ring-like aperture, 6 to 7 cm. in diameter, was encountered leading into a secondary pouch of approximately 10 to 12 cm. in diameter. The wall of this pouch was distinctly thinner and more flaccid than that of the uterus proper, and the placental attachment extended partially into it. Twelve and twenty-four hours later, the fundal irregularity was still demonstrable, thus excluding contraction ring. Convalescence was without untoward incident.

On February 26, 1930, bimanual examination was made, but as in examinations previous to conception, it was not possible to bring the corpus uteri between the examining fingers, and the palpatory findings were, consequently, indeterminate. However, on May 12, 1930, a hysterogram was made which showed definitely the bicornate nature of the uterus, and patency of the right tube.

800 Peoria Life Building.

HEMIPLEGIA COMPLICATING PREGNANCY

By Percy A. Perkins, M.D., F.A.C.S., Memphis, Tenn.
(*Obstetrical Service, Methodist Hospital*)

HEMIPLEGIA occurring during pregnancy is exceedingly rare. A search of the literature on this subject, dating back to the age of Hippocrates, revealed reports of only 43 cases. One of the best and most complete of these articles was contributed by Talley in 1924, at which time he was able to collect only 36 cases from the literature. In 1929 Scott's review of literature, including his own case, showed a total of 43 cases.

The paramount questions with which we were confronted in this case I am reporting were: what kind of brain lesion were we dealing with, and was toxemia a predisposing factor?

Mrs. J. E. C., para ii, aged 22, seven months pregnant, admitted to the hospital December 15, 1929. Her family history was negative. She gave a history of always having been healthy except that about three months before she had malaria and took ten grains of quinine daily for several weeks. Menstrual history normal. Last pregnancy and labor two years ago, normal except that she had some kidney trouble for a short while afterward. A few days before coming to the hospital she began to feel sleepy, dizzy, and a little nauseated. She had been on a milk diet for several days before admission to hospital.

On admission temperature was 98.6° F., pulse 94, blood pressure 104/68. She was complaining of dizziness, double vision, and nausea. Urine showed a faint trace of albumin and one or two pus cells. Total R. B. C. was 4,000,000, total W. B. C. 11,800, 81 per cent polys, urea nitrogen 14.5 per 100 c.c., negative Kahn test. Thompson, of the medical service, examined her and found her heart and lungs normal. His opinion was that this was a case of preeclamptic toxemia.

The following day her nervous condition was worse; she was mentally confused and disorientated. Blood pressure was 132/90, pulse 90, temperature normal, urine negative for albumin but showed four-plus acetone, CO_2 combining power 48.6 per 100 c.c. Dr. Ayres, of the obstetrical service, saw her in consultation and stated that she impressed him as a toxemic and advised a termination of pregnancy. During the next thirty-six hours she became worse, having delusions, seeing imaginary objects, and talking of killing some one. She was very noisy and hard to keep in bed. Chloral and bromides were not effective in controlling her, and it was necessary to add morphine. Pulse was 130. Labor was induced by bougie and packing; normal delivery twenty-two hours later of a normal five pound baby that died suddenly three hours later. About six hours after delivery the patient seemed to be in a stupor,

and there was a paralysis of the right leg, right arm, and right side of face. Pulse was 90, temperature 101° F., blood pressure 118/75. Apparently there was some pain when the right arm was moved or when pressure was made over left side of neck. Spinal puncture showed no increase in pressure. Many R. B. C., sugar 66 mg. to 100 c.c., cell count 30, but inaccurate on account of blood. Dr. Anthony examined her nose, throat, ears, and visual fields and reported them normal. Spinal puncture was repeated daily for four consecutive days and each showed blood present. Culture was negative. December 28 her condition was greatly improved, paralysis had disappeared, she had only occasional headache and was a little restless. Blood pressure 122/75, temperature 98° F., pulse 90. January 1 she was discharged. Her mind was clear, no paralysis was present, no headache.

Bunting, neurologist, saw her on several occasions and made the following report: "My examination of patient disclosed the following: patient in a delirium of combative maniac type. A right hemiplegia, complete, inclusive of right frontalis muscle. The spinal puncture disclosed a blood-tinged fluid—evenly tinged and which continued the even red color throughout the withdrawal of some 15 to 20 c.c. of fluid. The deep reflexes were less active on right. There was no Babinski or Oppenheim. Her speech on twenty-second or twenty-third showed a sensory-motor aphasia. Impression, a meningeal hemorrhage of left side which was probably helped by the frequent spinal drainages."

January 29 she came to my office, feeling fine, gaining weight, occasional pain in top of head. Urine was negative. Heart normal. X-ray of head negative. Blood pressure 125/85.

CONCLUSIONS

In my opinion this was a hemiplegia caused by a hemorrhage, probably meningeal. I also think that her symptoms were sufficient to justify us in the beginning to make a working diagnosis of preeclamptic toxemia. Even though the blood pressure was low, only a faint trace of albumin was found on two occasions and acetone once.

In view of the fact that we were unable to find any evidence of endocarditis, thrombophlebitis or any foci of infection, I conclude that there was some close association between her hemiplegia and toxemia and that possibly the hemiplegia was indirectly caused by, or the result of the toxemia.

528 Medical Arts Building.

A CASE OF PREGNANCY COMPLICATED BY MULTIPLE FIBROIDS OF THE UTERUS

Cesarean Section and Hysterectomy, With Child and Mother Surviving

By John Joseph Gill, M.D., F.A.C.S., Chicago, Ill.

IT IS not an uncommon occurrence to find a fibroid uterus retaining a pregnancy, but the case which I wish to present developed unusual features which are of sufficient interest to warrant its report.

On May 26, 1929, I was called to the home of Mrs. F., an American negress, who had for several months been under the care of a physician for dropsy. She had a marked generalized edema and the abdomen was enormously distended with fluid, blood pressure 180/150. She complained of blurred vision and epigastric pains. The urine was loaded with granular casts and albumin. She was thirty-eight years old and had been married fifteen years. She had not menstruated for six months, previous to which time her periods had been normal and regular; she had never before been pregnant and gave no history of venereal disease. The Wassermann reaction was negative, but smears from the vaginal glands were positive for gonococci.

Examination revealed a very large uterus with numerous large and small fibroids and a fetus of about six months' development.

Tincture of digitalis and magnesium sulphate were given in large doses, together with rest in bed and a regulated diet. The anasarca rapidly disappeared and general improvement became noticeable; blood pressure became gradually reduced and on June 29 registered 130/75. At this time, labor pains developed and the membranes ruptured. She entered the hospital but refused operative help for forty-eight hours.

On July 1, a midline abdominal incision was made. The panniculus was very edematous and about two liters of fluid was removed from the peritoneal cavity. The uterus was incised and a four-pound baby girl removed. The broad ligaments were clamped and a supravaginal hysterectomy performed, leaving the placenta intact. The mother and child progressed well and went home on the twenty-first day, postpartum. However, a few days later infection developed in the line of incision and a sinus persisted for ten weeks, when a tape end appeared at the surface and could not be removed. On September 16 she entered the hospital and under local anesthesia, a large laparotomy pad was removed. The sinus closed rapidly and the woman made a complete recovery. The baby at six months is doing well and weighs eight pounds.

Dr. Steward L. Vaughan, Pathologist, describes the uterus removed as follows:

The specimen is a uterus containing multiple fibroids which are chiefly subserous and intramural. The entire mass weighs 2382 gm., is roughly globular in shape and measures about 22 x 12 cm. in its largest diameters. The uterus is partially involuted, has a wall with an average thickness of 1½ cm. and the cavity is entirely filled with placenta. The umbilical cord appears normal. The diameter of the cervical canal at the internal os is 2½ cm. and the uterus was amputated at this point.

On the anterior superior surface of the uterus is a fibroid measuring 14 cm. in diameter which on section shows a wall varying in thickness from 3 mm. to 3 cm. and a cavity filled with a spongy degenerated material. Other fibroids scattered in the wall vary in diameter from 5 mm. to 6½ cm., calcification being present in many places.

5708 Harper Avenue.

A NEW OBSTETRIC FORCEPS*

By Professor E. H. Zweifel, Munich, Germany

THE forceps was devised by Hugh Chamberlain about 1640, but as he concealed the invention of his instrument, we regard Pollyn of Ghent as the constructor of the forceps in 1723. Since that time there have been many improvements. During the past fifty years, two instruments have been constructed on new principles. The one is the Tarnier which is meant to be used as high forceps. Despite its distinct advantages, it compresses the fetal head in a most dangerous way. The Tarnier forceps causes not only an immediate high fetal mortality but also many permanent injuries to the brain of the child. The Kjelland forceps was constructed with the idea of always applying it biparietally. Kjelland especially recommended his forceps for parietal bone presentation and applies the anterior blade in such a manner that it is rotated within the uterus. This technic seems to be not without

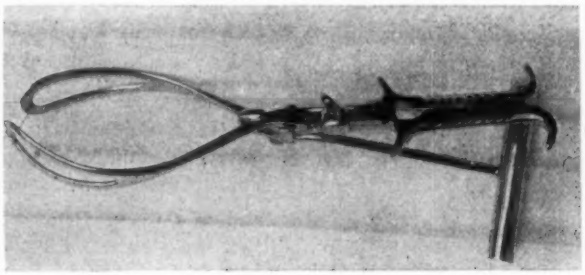

Fig. 1.

danger, as rupture of the uterus has been reported after the use of the Kjelland's forceps.

The construction of a new obstetric forceps was the outcome of a desire of mine to design a forceps which would combine in one instrument all the advantages of the modern models applied to the forecoming head.

The pelvic curve of this forceps is reduced to a minimum. The pelvic curve of obstetric forceps is practically superfluous with heads deep in the pelvis. When the head lies at a higher level, as for instance at the pelvic brim, it is a disadvantage. The same holds true for aftercoming heads.

For ordinary applications, this forceps is placed on the head just as the Naegele or the Simpson models. It can be applied in all diameters of the maternal pelvis and should always be applied biparietally to the child's head.

With high as well as with deep transverse heads, the new forceps can be brought to lie in the sagittal diameter of the pelvis, thus permitting a biparietal application. The particular advantage of the forceps lies in the fact that the

*Presented (by invitation) before the Chicago Gynecological Society, May 29, 1930.

first blade can be introduced along the lateral wall of the pelvis and rotated into position, as in the usual "wandering" technic. Thus, it is not necessary, as with the Kjelland instrument, to introduce this blade under the symphysis, carry it high up into the uterus, and twist it through 180° at that level. The "wandering" method of application has always been possible and, therefore, we could apply the forceps biparietally. The blades slide, one upon another, but can be locked in various positions by a fixation screw. This is of the greatest value in high forceps applications upon heads lying asymmetrically as in asynclitism. For such cases, the forceps is supplied with a traction hook, providing for axis traction. At the upper end of this hook is a "catch" which permits application from below in a very simple manner. At the lower end is a revolvable transverse handle, for applying the traction. In high-lying heads, the hook is drawn upon in the direction of the pelvic axis, just as with the Tarnier forceps. The extraordinary ease with which the traction hook can be attached and detached is of special value. (Fig. 1.)

In many cases, traction alone is sufficient and the head rotates spontaneously as it is brought down. When traction does not bring about rotation, the latter can easily be encouraged with the forceps. Used in this manner, the forceps is as suitable for normal positions of the head, as for those associated with high arrests, transverse, face and brow presentations and so on. It has been applied in hundreds of cases up to the present time in the Universitäts Frauen Klinik in Munich and in Berlin, in the Kantonsspital in Aarau, in the Hebammenschule in Bamberg and in many other clinics and by many practitioners, with excellent results.

In addition, it has been used in some cases of impacted breech presentation in order to draw the child's breech to the pelvic outlet, then the forceps is taken off and the extraction is performed with the fingers in the usual way.

Rouffart: Sympathectomy in Gynecology. Bruxelles méd. **10**: 232, 1929.

Rouffart, after a comprehensive discussion of the various aspects of sympathectomy in gynecology, draws the following conclusions:

We do not wish to advocate one method to the exclusion of other therapeutic measures. We wish only to show the value of this method despite the numerous unsettled points it possesses.

Hypogastric or preaortic sympathectomy is especially indicated in the treatment of pain in cancer cases. Resection of the superior hypogastric plexus is preferable in other cases. Both operations should be considered as sensory neurectomies. A sufficient resection of sympathetic connections causes a reduction of pain which proved unamenable in the other usual therapeutic measures, without affecting the harmony of the reflexes essential to vegetative life. These interventions have furthermore a hyperemic and trophic action capable of changing and cicatrizing hopeless lesions. But although they may be likened to sensory neurectomies, usually they are nothing more than complementary operations.

THEO. W. ADAMS.

Society Transactions

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF MAY 29, 1930

DR. IRVING STEIN presented a case of **An Unusual Ovarian Tumor.**

This woman, thirty-four years old, had a placenta previa with her third pregnancy. The child was extracted after version and there was a tear of the cervix up to the fornix. The child died.

For about two years, there were no symptoms of significance. The third year she had a very severe metrorrhagia. She had some pain in the left lower quadrant, a marked leucorrhea and a daily temperature of 99.5°.

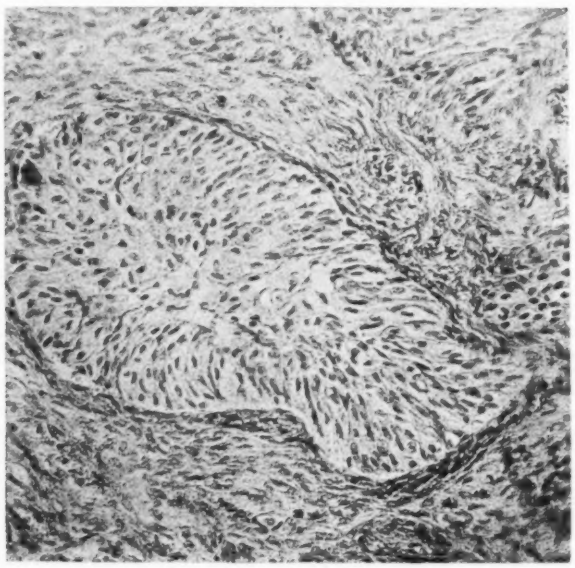

Fig. 1.

On admission, general examination was negative except for a chronic bronchitis. She had a tender ovarian swelling about 5 cm. in diameter apparently adherent to the apex of the cervical tear.

At operation a trachelorrhaphy and perineorrhaphy were first done. Then through a Pfannenstiel incision the peritoneal cavity was opened and an adherent, cystic ovarian tumor, 6 cm. in diameter was found. It was adherent in the culdesac just adjacent to the cervix, low down on the left side. The adhesions were broken up and the left tube and ovary and appendix were removed. The gross appearance at the time was that of a hemorrhagic corpus luteum cyst that was adherent in the pelvis. On microscopic examination, however, we found a rather peculiar looking area beneath this corpus luteum. In the middle of the ovary was a nodule a little less than a centimeter in diameter. A great number of sections were made, but a definite diagnosis was not established. Dr. Saphir's report is as follows:

Sections of the ovarian tumor revealed a definitely circumscribed area, just below a corpus luteum cyst, made up of clusters of epithelial cells. These groups or clusters varied in size, some large enough to cover the entire field. They were chiefly round, some oval and the individual cells were uniform in size and shape. (Fig. 1.) The cytoplasm stained lightly, nuclei centrally placed and vascular, and an occasional mitotic figure was seen. There was a resemblance of some of these cells to the carcinoma cells. There was a suggestion of alveolar arrangement with a moderate amount of stroma surrounding the clusters. In some sections were seen small circumscribed spaces stained pink, but no definite ova were recognizable in them. No definite invasion of the stroma was seen by the epithelial cells. There was also no evidence of gland formation. The remainder of the ovary contained a few cysts and one large corpus luteum with extensive hemorrhages within it. There was a slight increase in connective tissue in the ovarian stroma. In one part of the section, a few tubuli were recognizable which resembled remnants of wolffian duct structures.

Our first reaction was that it was probably a dermoid cyst, but there was no tissue to which that could be definitely identified, such as skin, hair, bone, muscle or cartilage, such as is found in dermoid.

Dr. Robert T. Frank and Dr. Klemperer diagnosed it as a wolffian duct inclusion.

DR. LOUIS RUDOLPH AND DR. A. C. IVY presented a paper entitled, **The Coordination of the Uterus in Labor.** (For original article see page 65.)

DISCUSSION

DR. IRVING F. STEIN.—In regard to the asynchronous contraction of the tubes in the cornua of the uterus, we have verified that with lipiodol in the human subject. Frequently, after the injection of lipiodol, the first manifestation was a closure of the tube ends. That we call a cornual spasm. The spasm begins in the cornua of the uterus rather than in the isthmus of the tube. Then we have seen one side open before the other. One may fill entirely before the other, or one may fill and the other remain empty. Some of those cases at laparotomy have been found to have patent tubes. I think that is what Dr. Ivy and Dr. Rudolph have shown, that there is asynchronous contraction of the tube. The contractions begin at the cornua of the uterus and are not always simultaneous.

DR. FREDERICK FALLS.—This work calls attention to the fact that the human uterus is fundamentally a bicornate uterus. If we watch for clinical evidence of bicornuosity in the human uterus, it will be found much more frequently than textbooks in obstetrics suggest. Several observations in the last few years have lead us to watch for this anomaly particularly. In these cases the uterus is found to be deflected either to the right or the left side of the body. When three-fourths of the uterus is to the right or the left, frequently labor will be found to give trouble. The contractions of the uterus are not normal in strength or frequency. The length of labor is usually prolonged but in some instances may be very much shortened. In addition to that, the baby may die during labor. In certain cases, the heart tones will be very rapid even before labor starts. In one case heart tones of 160 to 180 were observed before labor started. This baby died in the first stage with only 2 to 3 cm. dilatation, so it is not probable that there was any compression of the head. We have assumed that this is in some way due to defect in the circulation of blood in the placenta.

We should pay more attention to irregular uterine contractions and irregularly shaped uteri, and realize that the human uterus is frequently bicornate and that these uteri give rise to complicated labors.

It is very difficult to measure the strength of uterine contractions. Some years ago we tried to measure this by using a galvanometer to measure the action current that was generated by the contraction of the uterine muscle. We were successful in that.

DR. CARL HENRY DAVIS.—Some years ago one of the most prominent members of the American Gynecological Society confessed that he had done a cesarean section because of the presence of a fibroid, and at term failed to find any evidence of the fibroid. About that same time a patient was seen by Dr. Barrett and myself at different times, in whom another physician had made a diagnosis of fibroid and insisted that she be delivered by section. Neither of us could find the fibroid. The physiologic study reported gives us an explanation for these irregular contractions of the uterus which we sometimes find in early pregnancy and early labor.

DR. A. C. IVY.—It is well known that if you simply take out a strip of the uterus and put it in Locke's solution, it will contract rhythmically, just like a strip of intestinal muscle. Now, a possibility to which we did not refer is that it may be that this coordinated rhythm which we have shown to exist between the corpus uteri and the horn may be a fundamental property of the various portions of the musculature of the uterus. One has to stretch his imagination quite far, however, to imagine how one transverse section of the uterus will be timed with the remaining transverse portions. It is much more simple to think of some special coordinating mechanism, such as has been demonstrated by our experiments. The continuation of contractions by a uterine strip is analogous to those manifested by a strip of the stomach; but the contractions of a gastric strip are not analogous to normal gastric peristalsis.

In answer to Dr. Jones, we have cut both pelvic and hypogastric nerves and have removed the hypogastric ganglion.

DR. RUDOLPH (closing).—Our paper had to be abstracted so that we left out certain phases that related to the condition described by Dr. Davis.

In view of our theory of the bilateral origin of the uterus and its bilateral coordinating mechanism, it appears probable that unilateral relaxation of one side of the uterus and a normal tonus of the opposite occurs during pregnancy and labor, which we believe is the explanation of lateral obliquity of the uterus.

In a case that we report, a cyst-like protrusion occurred at the upper left quadrant of the uterus during the uterine contractions, and was associated with a left lateral obliquity of the uterus. In the interval, the uterus was symmetrical. After the bag of waters ruptured the uterus became symmetrical during the subsequent labor pains and labor progressed in a normal manner. We believe that this condition is due to a change of tonus of the two halves of the uterus; the right half contracting in a normal manner, while the left half of the uterus was in a state of paresis and a paralysis of the corresponding orbicular muscles of Ruysch which accounts for the cyst that appeared and the left lateral obliquity of the uterus during the labor pains before the bag of waters ruptured.

DR. ZWEIFEL presented **A New Obstetric Forceps**, see page 138.

Department of Maternal Welfare

CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

A SURVEY OF MATERNAL DEATHS IN MARYLAND*

BY J. H. MASON KNOX, PH.D., M.D., BALTIMORE, MARYLAND
(Chief of the Bureau of Child Hygiene, State Dept. of Health)

A SURVEY of the maternal deaths occurring in the counties of Maryland, exclusive of the city of Baltimore, during the last three years, 1927, 1928, and 1929, has just been completed.

In addition to Baltimore there are but four cities in the State having a population in excess of 10,000. The study, therefore, comprises principally information concerning the women who died in childbearing in the rural and small town areas.

The information on which the survey was made was obtained through personal interviews, by two experienced women physicians, with the practitioners concerned, for the 1927 and 1928 cases and by the same method by local health officers in 1929.

Maryland has a lower maternal mortality rate than many of her sister states. The rate for the Birth Registration Area in 1927, the latest published, was 6.5 as compared to 4.95 in Maryland.

It is thought, therefore, that the results of this study in rural Maryland may be of general interest and may fairly represent conditions prevailing in many other states.

The fatal cases investigated were 241 in number, occurring in 47,515 live births, giving a maternal mortality rate in rural Maryland of 5.06 per 1,000 live births.

Cause of Death.—The primary causes of death in the 241 cases reviewed were:

Accidents of pregnancy, abortion, ectopic gestation (143)*	27	11.0%
Puerperal hemorrhage (144)	36	14.9%
Other accidents of labor including cesarean section, difficult labor, ruptured uterus (145)	19	7.8%
Puerperal septicemia (146)	82	34.0%
Puerperal phlegmasia alba dolens embolus, sudden death (147)	10	4.0%
Puerperal albuminuria and convulsions (148)	67	27.8%
	241	99.5%

*Refer to International list of causes of death.

It is to be noted that puerperal sepsis and albuminuria and convulsions together caused the death of 149 women, or 61.8 per cent of the whole number.

Sixty-five of these deaths, or 27 per cent of the 241 cases, occurred in association with an interruption of the pregnancy before the seventh month; that is, with abortion or premature birth.

*Read at the Annual Meeting of the Medical and Chirurgical Faculty, Baltimore, Md., April 23, 1930.

The primary cause in this group is indicated below:

Accidents of pregnancy, abortion, ectopic gestation (143)	21	32.4%
Puerperal hemorrhage (144)	3	4.6%
Other accidents of labor including cesarean section, difficult labor, ruptured uterus (145)	0	
Puerperal septicemia (146)	33	50.7%
Puerperal phlegmasia alba dolens embolus, sudden death (147)	0	
Puerperal albuminuria and convulsions (148)	8	12.3%
	65	100 %

In these instances of a prematurely i upted gestation the incidence of sepsis is extremely high; 50 per cent.

These figures would indicate that in general the dangers to the mother from the most feared complication of pregnancy are materially increased when the gestation is interrupted before term and that such a procedure should be undertaken only under the direction of skilled medical advice.

Attendant at Birth.—The attendant at birth is shown in the accompanying table together with the primary cause of death, in cases of seven months or more gestation:

TABLE I

	TOTAL	ACCIDENTS OF PREGNANCY	HEMORRHAGE	OTHER ACCIDENTS OF PREGNANCY	SEPTICEMIA	ALBA DOLENS	ALBUMINURIA	OTHERS
Maternal deaths	176	6	33	19	49	8	59	2
Attended by phys. alone	145	6	26	18	38	7	49	1
Physician after midwife or other attendant	14	0	3	0	6	1	3	1
Midwife alone	8	0	2	0	4	0	2	0
Other attendant or none	9	0	2	1	1	0	5	0

Only those cases which died after seven months gestation are included—176 in number. For this group there should have been ample time to make arrangement for the prenatal care of the mother and for the conduction of labor.

Special effort was made to ascertain those cases in which a midwife or other attendant preceded the doctor in the care of the patient.

The surveys show that a large proportion of these 176 women, 145 or 82 per cent, were attended by physicians alone, and that in 14, or 8 per cent of the cases, the physician was called after a midwife or other attendant had been in charge, while in 17 instances or 10 per cent the patients were delivered by midwives alone or were delivered with no attendant.

It is to be noted that among the women whose pregnancy lasted more than seven months, 108 or 61 per cent of the deaths were due to septicemia and albuminuria.

Race.—In 241 deaths in the counties of Maryland, 164 occurred among white women and 77 among colored women, the maternal mortality per thousand live births for these groups being 4.1 for white and 8 for colored.

Age.—Analysis of our cases according to age indicates that 94 of these deaths occurred among women between twenty and thirty years of age, and 78 between thirty and forty, that is 71 per cent were between twenty and forty years of age. There were 172 deaths in women in their early prime when they should have had a long life expectancy.

Social Status.—Among our 241 cases, 215 or 89 per cent were married, 26 or 11 per cent were not married. Of the 164 white women, 158 or 96 per cent were married; 6 or 4 per cent were unmarried, and of the 77 colored women, 57 or 74 per cent were married and 20 or 26 per cent unmarried.

Previous Children.—One hundred fifty-nine or 66 per cent of the deaths occurred among women who were mothers of older children who were left in the home bereft of the mother's care. These facts seem tragic enough to arrest attention and should lead to some concerted professional or community action to reduce the unnecessary deaths among women so greatly needed.

Prenatal Care.—Inquiry was made in each case as to the kind of examination and medical attention the patient received before delivery. When this comprised a general examination including that of heart, lungs, abdomen, measurement of the pelvis in primipara, examination of urine and determination of blood pressure not later than in the seventh month of pregnancy, such prenatal care was designated as "good." Some attention to the patient less than above summarized was called "inadequate" prenatal care.

Of 176 women who died after seven months or more gestation, 15 or 8 per cent received good prenatal care, 63 or 35 per cent received inadequate prenatal care, and 98 or 56 per cent received no prenatal care. In the series of 176 women who died after pregnancy of seven months, measurement of the pelvis was reported in but 18 instances and the Wassermann test was made in only 5 cases. The value of prenatal care in reducing maternal and neonatal mortality and in lessening the number of stillbirths is so well understood that no additional proof or argument in its favor is necessary.

Dr. Dublin, statistician of the Metropolitan Life Insurance Company, estimates that the lives of two out of every three American women who die each year during pregnancy, in childbirth, or shortly thereafter, could be saved if they received medical and nursing care. This means that at least 10,000 of the 15,000 deaths among women from some complication of childbirth in the United States are preventable.

Hospital Deaths.—In our series of 241 fatal cases death occurred at home in 108 instances or 44 per cent and in a hospital in 133 instances or 55 per cent. It should be stated, however, that in nearly every one of these hospital deaths the patient's symptoms began at home and she was brought to the hospital in a critical condition and that the aid of the hospital was sought because of urgent symptoms of which the attending physician had learned for the first time immediately before bringing the patient to the hospital.

SUMMARY

It must be evident from these figures which have been briefly summarized that a considerable number of women in the last three years lost their lives in the counties of Maryland without satisfactory care before or during childbirth.

These women are for the most part not the very young or the old in years, but in the majority of instances the lives that were lost were those of married women living in normal homes and frequently mothers of older children. In other words, they comprise a group that cannot be lost without great loss in many ways to their families and to the communities in which they lived.

A surprisingly large percentage of the deaths resulted from premature births among women who had not been under medical advice.

Careless and ignorant midwives were associated with these maternal deaths in only a small proportion of these cases.

The impression we have received from this review of maternal deaths in the counties of Maryland is that they were due directly or indirectly to the ignorance

or indifference of the people themselves. Help from physician or midwife was rarely called for until alarming and dangerous complications had arisen and the physician was obliged to take emergency measures under unfavorable conditions. The patients who were reported to have died in hospitals were almost without exception admitted extremely ill when there was but little that could be done to save them.

The apparent acceptance on the part of families and the public of the many deaths in childbearing as a matter which cannot be changed, deserves serious consideration. For until this attitude is altered and it is recognized generally that when a woman is in competent hands early in her pregnancy the dangers of childbearing are greatly lessened, we shall continue to lose many lives unnecessarily.

Certainly it is most desirable that those undertaking obstetric work should have adequate training and experience. This matter is receiving attention by many medical faculties.

However, a review of the maternal deaths here presented shows that but few of them could have been saved by more skilled hands at the critical period in which the physician was first called. Already sepsis or toxemia or other complication was so far developed as to render the best treatment unavailing.

We were not able to determine in our series how much of the delay in calling in a doctor was due to the desire to save money. This seems to have been a factor in a considerable number of instances. Certainly the usual fee in the counties for obstetric service is a moderate return for the value of this service. Moreover, it is a charge which can be anticipated and saved for, as is not true of sudden or unexpected illness. We are told, however, that the cost of illness cannot be defrayed out of the available income in the case of about one-third of the American homes and presumably this is true also of the cost of bearing children. When the dangers of procrastination *are not understood,* the doctor's services are dispensed with as long as possible.

Obstetric service is provided free of all charge by private practitioners in many instances, greatly to the credit of the physician; but this is not fair to either doctor or patient who may not want to be a receiver of charity.

In the rural sections there is no obstetric service available to the indigent such as is offered to the corresponding group in Baltimore through the Johns Hopkins Hospital and the Hospital of the University of Maryland and other clinics. Hospital beds, free or at moderate cost, are provided in the county hospitals. There is still much unwillingness to make use of them for normal cases. If there were a general demand for such accommodation, the beds would prove far too few.

It would seem then that there is need in each county for some organized plan by which obstetric service could be furnished at little or no cost to those families of very moderate means. From such families come most of our maternal deaths at present.

It is hardly reasonable to expect a physician whose practice covers a large area to undertake gratis the care of widely separated normal obstetric cases. If the private physician is to continue to do this charity work, he should receive from the county or elsewhere an adequate financial return.

It is the custom of a number of doctors in the counties to use midwives whom they know to be capable and clean in their obstetric practice among the poor.

The midwife in Europe, as is well known, occupies a more important position than with us. There she delivers nearly all normal cases and calls upon the physician only when difficulties arise.

Our midwives in Maryland are far below those in Europe in education and training. However, the older ones are dying out and the newer ones have had some instruction and have passed a qualifying examination. The standard among them

would be greatly raised if a carefully selected number could be received in some of our county hospitals and given instruction and practical experience. This could be arranged with but little expense to the hospital.

It is conceivable that a physician with an active obstetric practice might make use of three or four midwives resident in different communities covered by his practice for delivering normal cases under his supervision. It would be advisable that he make at least one complete physical examination and be ready to respond if unforeseen difficulties appeared.

There are now public health nurses in every county who are willing to visit any indigent expectant mothers at the request of a physician, give them such prenatal instruction as the physician desires and report to him at regular intervals. In two counties prenatal clinics have been organized with the approval of the profession for the examination and advice of indigent expectant women.

We have received monthly reports from one of those prenatal clinics. The patients are either referred by local physicians or are indigent women, found by the public health nurses, who had made no arrangement for their care before or during labor.

Of some 50 of these cases at least 10 were suffering from conditions which probably would have resulted fatally except for the care received at the clinic. Thus far there have been no maternal deaths.

Would it not be possible in each county for the physicians themselves, or if they desire it, with the assistance of an experienced obstetrician, to organize a similar clinic where indigent expectant mothers may be examined early in their pregnancy, receive prenatal advice, and be helped to make suitable arrangements for their labor? To such a clinic the local physician might care to refer certain of his own patients and examine them himself. Probably many midwives could be encouraged to send their patients to such a clinic for examination and prenatal advice. A regular prenatal clinic in a county could readily be made a useful teaching center for physicians and so of mutual advantage both to the patient and to the profession.

It has been suggested that a wider use in the counties of maternity insurance would bring improvement to the conditions it is so desirable to remedy. It is to be feared, however, that the group it seems especially necessary to help, would not be willing, perhaps not able, to pay the necessary premiums. It is quite evident that the profession cannot be, and the public ought not to be, satisfied with the present state of affairs.

Through some plan, such as the more frequent use of the county hospital, the use and supervision of selected midwives, the prenatal clinic, maternity insurance, or the employment of the public health nurses, the physician might be able to supply at less sacrifice of his own valuable time and at less financial cost to his patient of moderate means, satisfactory prenatal and natal care, both of which seem desirable from the study of the maternal deaths.

The fundamental part of any plan, however, for better service, is the necessity of bringing home to each prospective father and mother in the State, and to every community, that not to attempt to furnish every expectant mother with at least a minimum of medical care during her waiting period and at the hour of labor, is little short of criminal negligence.

It is recognized that excellent and early care of the expectant mother and skilled obstetric service will not save all women in childbearing, but it is confidently believed it would result each year in the salvage of one-third of the lives of mothers, and one-third of the potential infant lives now being lost before or shortly after birth. This is certainly a goal worth striving for.

American Journal of Obstetrics and Gynecology

GEORGE W. KOSMAK, M.D., EDITOR HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

Editorial Comments

Certification of Specialists

ATTENTION has already been called in our pages to the organization of the American Board of Obstetrics and Gynecology, created for the purpose of determining the competency of specialists in obstetrics and gynecology. The capabilities and proper designation of a specialist are matters which concern the public as well as the medical profession. With the enormous growth in medicine during recent years, it is obviously impossible for any one individual to familiarize himself with all the diagnostic refinements and therapeutic methods utilized in its various branches; hence, a demand for specially qualified practitioners is the logical sequence of such a state of affairs. Naturally difficulties have arisen in distinguishing between those who have been thoroughly trained, and those who have not. Thus far, so-called specialism has been practically uncontrolled. Sufficient contact with the general practice of medicine, so essential as a balance wheel for the potential specialist, has been largely disregarded. Internes graduated from one or another hospital service are all too ready to restrict their practice within the confines of some special field of medicine, or men in general practice go to a postgraduate school for a course which is all too brief, or perhaps spend a year abroad, and then pose as qualified specialists despite the inadequacy of their preparation.

The State makes no effort to standardize qualifications for the specialist: it grants a license which empowers its holder to practice any or all branches of medicine, and after that leaves the matter of his professional activities entirely to chance. Fortunately, many men have seriously fitted themselves for specialism by long service in an accredited hospital and under the supervision of competent teachers, as well as by wide clinical experience and intensive study and reading. But there have been few or no standards established whereby the pub-

lic at large can determine the individual's proficiency, except those set up by certain bodies whose membership represents national medical societies and who have seen the need for action. The task of fixing even minimum requirements for the average practicing specialist is a difficult one, and every credit should be given to those groups who are attempting to solve what only a short time ago seemed like an impossible problem. The ophthalmologists, the otologists, and the laryngologists have constituted themselves a vanguard with which the obstetricians and gynecologists have now joined ranks, in an effort to do for American medicine what no governmental agency can well undertake. Such reforms emanating from within the ranks of the profession itself will undoubtedly contribute more largely to public confidence than would any legislative action.

The American Board of Obstetrics and Gynecology was launched last September and is now actively functioning. It is composed of three representatives from each of the three national groups interested in obstetrics and gynecology: the American Association of Obstetricians, Gynecologists and Abdominal Surgeons; the American Gynecological Society; and the Section on Obstetrics and Gynecology of the American Medical Association. The members of the Board are to be congratulated on the rapidity with which they have formulated their plans and regulations, and have begun the actual work of certifying specialists by examination and otherwise. During the early period of the Board's career trivial errors may be made, and perhaps certain details may meet with criticism, but its objectives are so meritorious and worthy of support by the profession that patience in the adjustment of details must be exercised until the project is well stabilized. Proper recognition of its undoubted value by the lay public and medical profession alike is inevitable.

Intensive Prenatal Care

WITH the growth of medicine and the recognition of the fact that good health is a matter of public as well as of individual interest, there have been developed many now widespread social welfare activities by lay and governmental agencies. Tuberculosis, heart disease, the infectious diseases of childhood, cancer and, naturally, because of its sympathetic appeal, childbearing, have all served as nuclei for specific organizations which have been most helpful and important in the solution of many medical problems. To these organizations there must be given much credit for the success attained in lowering the incidence and mortality of many of the more widespread illnesses, and this applies likewise to the complex problems associated with any hoped for improvement in the mortality and morbidity associated with childbearing. Perhaps the most extensive and noteworthy movement of the kind in this country has been the attempt by the federal government to

develop a nation-wide interest in this field through the medium of the Shepard-Towner Act, and more recently the White House Conference. The former failed for lack of continued appropriations by Congress. It was never convincingly successful because the measure violated certain structural relations in our government and for other reasons that need not be discussed here, but the propaganda associated with the same did arouse the national conscience.

The recent White House Conference has served to continue this interest and it is unfortunate that the occasion should have been made use of to launch a propaganda for a separate Children's Bureau rather than to have this activity as part of a policy of unified health control. True the child is an entity but he and his problems are closely related to his environment and in the latter his mother plays an important part. Therefore the preservation of her maternal functions must likewise be regarded as an essential link in the chain of obstetric supervision, which includes watchful care over all of the stages of pregnancy rather than the imposition of any one inclusive remedy. The good results of such supervision have been most satisfactorily demonstrated by the work of certain well-organized groups, of which the Maternity Center Association of New York forms a conspicuous example. A detailed report of the activities of this Association was published in the December issue of the JOURNAL, and shows in very dramatic fashion that intensive prenatal care associated with correspondingly satisfactory attendance during labor will produce results that are worthy not only of commendation but should serve as a stimulus for emulation in other places.

Such community developments, with local responsibility and interest as guiding factors, will do more than any centralized governmental agency to bring about that needed consciousness among our people for the best possible obstetric care obtainable. When it can be demonstrated that in a group of 5000 mothers cared for by this Association during an eight-year period, the mortality was about one-third of that in the same area among other women, with a reduction in stillbirths of over 40 per cent and of infant deaths of over 30 per cent as compared with the control groups, there should be no question of the value of such services. And these results have very definite implications for they show the need of similar machinery elsewhere. In this connection attention may be called to an estimate made by Dr. Louis I. Dublin, the well-known statistician, that the lives of two out of every three American women who die each year as the result of childbearing could be saved if they received satisfactory medical and nursing care, which means that two-thirds of these deaths are preventable. This is a challenge that the medical profession should not be slow to accept.

Department of Reviews and Abstracts

Conducted by Hugo Ehrenfest, M.D., Associate Editor

Selected Abstracts

Fetal Injuries

Freund and Schmitt: The Influence of Ultraviolet Irradiation of the Mother on the Constitution of the Newborn. Monatschr. f. Kinderh. 43: 424, 1929.

The authors employed the quartz lamp in increasing doses from two to twenty minutes on a series of pregnant women, using every other patient admitted to the clinic as control. The irradiation was continued throughout the period of pregnancy and varied from one-half to twelve hours in toto according to when the patient presented herself. The children subsequently born were studied as to differences in length, in weight, relationship of head circumference to chest circumference, the development of rickets as shown by x-ray and clinically, and differences in blood phosphates. The results were as follows: Those who received irradiation showed an average increase in length of 0.6 cm. Of these, children born during the winter months, October to April, showed an increase of 1.3 cm. while those born during the summer months, April to October, showed only a 0.09 cm. increase. In weight the average difference was 97 grams, with a corresponding increase to 213 grams during the winter months for those irradiated. The relationship between head and chest circumference in both groups did not vary sufficiently to warrant conclusions, and the cases studied as to onset of rickets were too few. Of 13 irradiated cases studied for blood phosphates 7 were above normal, 4 normal, and 2 below normal. Of 8 cases not treated, 2 were above normal, 3 normal, and 3 below normal.

The authors believe that although their study has been of short duration and in relatively few cases, there is a distinct superiority shown in children whose mothers have been irradiated antepartum, especially in those children born during the winter months.

Frank Spielman.

Unterberger: Damage to the Fetus through Repeated Exposures to Roentgen Ray During Pregnancy. Zentralbl. f. Gynäk. 53: 44, 1929.

The article is based on a single case, a woman aged forty-three, who had been under the writer's care for years. She had had infantile genitalia when first seen. At thirty-nine she was a primipara, at which time she had a gastroenterostomy done during the third month of pregnancy for a bleeding peptic ulcer. This pregnancy and the succeeding one resulted in normal offspring. About the third or fourth month of the third pregnancy, the patient again had marked gastric symptoms, and had a series of x-rays after an opaque meal for diagnostic purposes. Gastric carcinoma was suspected, but at laparotomy it was found that the defects observed in the plates were caused by numerous dense adhesions. These were freed, and postoperatively another series of x-rays was taken. Soon a low grade hydramnios developed. The patient delivered about 4 weeks prematurely a small fetus which

lived only five minutes, after an unusually long labor which was terminated by forceps. Postmortem examination of the fetus showed an anasarca and general evidences of underdevelopment in all the thoracic and abdominal viscera. The blood showed a distinctly fetal type of cells. Neither the child nor the parents had any evidences of syphilis or nephritis. The author concludes from this that the condition of the fetus was due to the repeated exposure to the roentgen ray, and he is sustained in this view by Prof. Kaiserling, who did the autopsy on the fetus. Therefore, the author emphasizes that special care should be used in similar cases.

WILLIAM F. MENGERT.

Doederlein: Radiotherapy and Progenity. Deutsche med. Wchnschr. 54: 1997, 1928.

The author reports 11 cases of conception and delivery of healthy children after a varying period of amenorrhea produced by radiation (x-ray and radium).

"Should this experience of the birth of healthy children after late conception following radiotherapy be generally confirmed, then the objection against temporary sterilization would be overcome and great possibilities for a new therapeutic procedure become evident."

GRUENFELD.

Fischer: Radiotherapy and Progenity. Deutsche med. Wchnschr. 55: 89, 1929.

The author warns the profession, on the basis of theoretic consideration and experimental experience, to regard radiation as nondetrimental to the offspring, because the first generation has not shown anomalies.

Damage to the germ may show in later generations or may become evident when two individuals with non-evident radiation-damage to their generative cells should procreate children. This theoretic criticism is the application of the Mendelian laws to the problem whether and when a damage to the ovum by radiation will become evident.

Experiments on mammals have not yet been carried out in a conclusive way to prove or disprove that radiation is innocuous to the progenity.

GRUENFELD.

Peig, J. C.: Diversity of Invasion by the Treponema in a Case of Twins. Revista espan. de obst. y ginec. 14: 152, 1929.

A secundipara with strongly positive Wassermann reaction had a premature infant in her first pregnancy which died of meningitis when 8 months old. Her second pregnancy was complicated by hydramnios and terminated in the birth of twins. The first fetus weighing 1600 grams was dead and macerated. The second weighing 1300 grams was born alive but survived only thirty hours. There were two placentas and two distinct sacs. The macerated fetus showed the luetic stigmas to a marked degree, and examination of its liver pulp revealed spirochetes. The other showed only slight evidence of the condition, and liver pulp examination was entirely negative. The placenta of the first was discolored and edematous, the second apparently normal.

The author explains the difference in intensity of the reaction in the fetuses partially on the basis of a greater resistance of the placental filter in one of them. The main reason lies in the different physicochemical composition of the twins, each of which, since they arose from different ova, must be regarded as being a distinct individual capable of a different response to the infection.

FRANK SPIELMAN.

Klaften, E.: The Treatment of Newborn Infants of Syphilitic Mothers, Arch. f. Gynäk. 134: 88, 1928.

There is a tremendous mortality from syphilis during the first three months of life which can be materially reduced by means of systematic treatment both during pregnancy and in the first weeks of extrauterine life. Of the children born of mothers who had active secondary syphilis during their pregnancy 90 per cent can be kept alive by active and intensive antiluetic treatment and 75 per cent of such children will, if properly treated, never show any evidences or symptoms of syphilis. Even if the syphilitic infection in the mother be a latent one, the child should immediately be subjected to active antisyphilitic treatment with arsphenamine, bismuth, etc. Klaften treated 48 apparently healthy children of mothers suffering from latent syphilis and of these only two died. Three others developed syphilis in spite of the treatment and 43 remained healthy and exhibited negative serum reactions. Of 84 children of mothers with latent syphilis who were not given antiluetic treatment, only 46 were alive and free from syphilis after three months.

The newborn infants tolerate comparatively large doses of arsphenamine very well. Those infants who do not react well show evidences of luetic changes in the organs in spite of the treatment and due to the spirochetal invasion.

RALPH A. REIS.

Arbat: New Methods in the Treatment of Hereditary Lues. The Activation of the Specific Therapy by Transfusion. Revista espan. de obst. y ginec. 14: 155, 1929.

The results obtained in the newborn with antiluetic treatment are not nearly as good as those obtained in the adult. The reason for this is to be found in the inability of the newborn organism to respond to specific treatment. The therapeutic coefficient of the various preparations of mercury, arsenic, and bismuth depends on the activation of the drugs, a factor determined by the organism. As proof of this there is the fact that different effects are obtained with the same preparations in different patients. Also, the effects of cutaneous proteid injections vary.

In the hope of producing a better response to therapy the author combines whole blood with the preparation used and injects the mixture. The advantages to be derived from this method are activation of the product by the ferments of the blood, and an increase in the natural defensive power of the organism by the transfusion. The injections are made into the muscle every three days after the first, and every four days after the seventh injection. Sulfarsenol in increasing doses from ⅛ centigram to 2 centigrams per kilo body weight is mixed with mother's blood in quantities varying from ½ to 1 c.c. The anticoagulant property of the arsenicals is an aid in using this method.

The only untoward effects observed in a considerable number of cases have been transient icterus and slight temperature. The results have warranted its continued use.

FRANK SPIELMAN.

Gammeltoft, S. A.: A Case of Encephalitis Hemorrhagica After Salvarsan Treatment During Pregnancy. Acta obst. et gynec. Scandinav. 9: 167, 1930.

The author reports a case of hemorrhagic encephalitis which followed the administration of salvarsan to a pregnant woman and he compares this case with three similar cases observed in Denmark. He emphasizes that even though this danger is slight, the treatment of syphilis during pregnancy should be supervised by specialists because they alone can detect the early signs of harm done by salvarsan.

J. P. GREENHILL.

Correspondence

Extension Courses

To the Editor.—There is much to commend in the plans of "extension teaching in obstetrics" recently suggested by Dr. James R. McCord (this Journal, November, 1930) and Dr. E. D. Plass (*J. Iowa State Med. Society*, April, 1930). It is very evident that these teachers appreciate their great responsibility. However, it is equally apparent that their efforts do not entirely meet the requirements. There is no short cut to knowledge, and least of all, in obstetrics. Either a man "knows his stuff" or he does not know it. Either he is, or he is not, an obstetrician.

The art and skill required to qualify in this capacity are not learned in a few hours. We regard as misleading and pernicious the absurd implication that several standards of obstetric practice must necessarily prevail in this country. To receive every aid that modern medicine affords is the "divine right" of every "woman with the badge of maternity upon her." The fact that nineteen out of every twenty women would deliver themselves without or in spite of any artificial aid, only tends to obscure the principle involved.

Moreover "our statistics" will not improve until it is frankly acknowledged and frequently emphasized by "leaders of the profession" that the art of obstetrics including gynecology, is an interesting, comprehensive, and an exacting specialty worthy of any man's entire time, talent, and skill.

Extension teaching should include, moreover, at least one short intensive demonstration in general practice. Recent graduates are habitually urged to locate in remote rural districts. In this situation they are enjoined to practice medicine and surgery. There is no doubt that it would be instructive to observe just how a "professor" would react when asked to deliver modern medicine, in all its manifold clinical and technical complexities, at the bedside of patients. If tragi-comic incidents could be avoided such a course would be extremely helpful and popular.

NICHOLAS SCHILLING, M.D.

NEW HAMPTON, IOWA.

Item

Announcement of Examinations by the American Board of Obstetrics and Gynecology

The following announcement has been received from the Secretary of this Board:

"The written examination must be taken by all applicants classified in Group 3 (see booklet), and will be held on Saturday, March 14, 1931, at 2 P.M. in the following cities:

New York City	Boston, Mass.
Chicago	Grand Rapids, Mich.
Philadelphia	Baltimore, Md.
Toronto, Ontario	Atlanta, Georgia
Indianapolis, Ind.	Cincinnati, Ohio
Portland, Oregon	San Francisco, Cal.
Rochester, Minn.	Grand Forks, North Dakota
Iowa City, Iowa	Denver, Colorado
St. Louis, Mo.	Galveston, Texas

Raleigh, North Carolina

"This examination will consist of ten questions pertaining to obstetrics and gynecology, and a rating of 75 per cent will be required. Each candidate for Group 3 also will be required to submit typewritten reports on a total of fifty (50) obstetrical and gynecological operations which he has performed, and these case records are to be presented with his examination paper to his local examiner on March 14.

"The practical, or oral, clinical and laboratory examination will be held in Philadelphia, Pa., on Saturday, June 6, 1931, commencing at 9 A.M. and will be given to all applicants in Group 2 and Group 3. The candidates will be expected to identify and discuss three or four common obstetrical and gynecological pathologic specimens and the histologic sections taken from them. The clinical part of the examination will be conducted in a hospital where an individual case will be discussed in detail with each candidate. An endeavor will be made to adapt the details of the oral examination to each candidate's previous experience and practice, and will be particularly directed to ascertain his familiarity with recent obstetrical and gynecological literature, the breadth of his clinical experience, and his general qualifications as a specialist in obstetrics and gynecology.

"Each candidate in Group 3 will be expected to appear before the examiner or assistant examiner in the territorial district in which the candidate resides, unless special arrangements otherwise have been made in advance through the Secretary, for the written examination on March 14. He should notify the Secretary before February 21 as to which of the two cities of his district he will present himself for examination, so that his credentials may be forwarded to the proper examiner in advance. The territorial districts, the examiner's names, and the places of examination appear below.

"In each instance the examination papers and case records will be sent to be reviewed and marked by an examiner in another district from that in which the candidate resides and tries his examination.

TERRITORIAL DISTRICTS

1. New York; Maine; New Hampshire; Vermont; Massachusetts; Rhode Island; Connecticut.
   Examiner: Dr. Walter T. Dannreuther, New York City.
   Ass't Examiner: Dr. Louis Phaneuf, Boston.
2. Illinois; Michigan; Wisconsin.
   Examiner: Dr. Fred L. Adair, Chicago.
   Ass't Examiner: Dr. Alex. Campbell, Grand Rapids, Mich.
3. Pennsylvania; New Jersey; Delaware; Maryland; Virginia; West Virginia; District of Columbia.
   Examiner: Dr. Edward A. Schumann, Philadelphia.
   Ass't Examiner: Dr. Edward B. Richardson, Baltimore.
4. North Carolina; South Carolina; Georgia; Florida; Alabama; Louisiana; Mississippi.
   Examiner: Dr. Paul Titus, Pittsburgh, Pa.
   Ass't Examiner: Dr. J. R. McCord, Atlanta, Georgia.
   Raleigh, North Carolina (subject to possible change to Atlanta).
5. Ohio; Indiana; Tennessee; Kentucky.
   Examiner: Dr. Joseph L. Baer, Chicago, Ill.
   Ass't Examiner: Dr. Magnus A. Tate, Cincinnati, Ohio.
   Indianapolis, Ind. (subject to possible change to Cincinnati).
6. Washington; Oregon; California; Nevada.
   Examiner: Dr. Jennings Litzenberg of Minneapolis, Minn.
   Ass't Examiner: Dr. Frank W. Lynch, San Francisco, Cal.
   Portland, Oregon (subject to possible change to San Francisco).

7. Minnesota; North Dakota; South Dakota; Idaho; Montana; Wyoming.
   Examiner: Dr. R. D. Mussey, Rochester, Minn.
   Ass't Examiner: Dr. J. H. Moore, Grand Forks, North Dakota.
8. Iowa; Nebraska; Colorado; Utah.
   Examiner: Dr. E. D. Plass, Iowa City, Iowa.
   Ass't Examiner: Dr. C. B. Ingraham, Denver, Colo.
9. Missouri; Kansas; Nebraska; Arkansas; Texas; Arizona; Oklahoma; New Mexico.
   Examiner: Dr. G. D. Royston, St. Louis, Mo.
   Ass't Examiner: Dr. W. R. Cooke, Galveston, Texas.
0. Canada.
   Ass't Examiner: Dr. William B. Hendry, Toronto, Ont.

"The practical or oral examination in Philadelphia on June 6 is scheduled to precede by one day the annual meeting of the American Medical Association.

"Candidates in Groups 2 and 3 will report to the entire Board in Philadelphia on June 6 through the direction of Dr. Edward A. Schumann of Philadelphia.

"Candidates will be notified later of the exact address at which their examinations will be held.

"For all further information address the Secretary, Doctor Paul Titus, 1015 Highland Building, Pittsburgh, Pa."